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DATE: Wednesday, October 13, 2004

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☐	L10	L9 and (oscillat$4)	29
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☐	L8	L7 and ((compensat$4 or control$4 or correct$4 or cancel$4 or cancellation or cancelation or remov$4) with (magnet$4 with (field or strength or flux or flucuat$4 or varies or varied or varying or vary or chang$4 or alter$4 or modif$4 or adjust$4)))	1268
☐	L7	L6 and (magnet$4 with (field or strength or flux or flucuat$4 or varies or varied or varying or vary or chang$4 or alter$4 or modif$4 or adjust$4))	3733
☐	L6	L5 and (measur$4 or determin$4 or determination or estimat$4)	28436
☐	L5	L4 and (temperature or heat$4 or thermal$4)	31652
☐	L4	L3 and (compensat$4 or control$4 or correct$4 or cancel$4 or cancellation or cancelation or remov$4)	37256
☐	L3	L2 and ((energiz$4 or suppl$4 or electric$4 or power$4 or appl$4 or current or provid$4) with (gradient or "Gx" or "Gy" or "Gz" or "Gp" or "ge" or "gs" or (gradient with coil)))	40043
☐	L2	L1 and (gradient or "Gx" or "Gy" or "Gz" or "Gp" or "ge" or "gs" or (gradient with coil))	166767
☐	L1	((magnetic adj resonance) or MRI or NMR)	188828

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Search Results - Record(s) 1 through 17 of 17 returned.

☐ 1. Document ID: US 20040169513 A1

Using default format because multiple data bases are involved.

L11: Entry 1 of 17 File: PGPB Sep 2, 2004

PGPUB-DOCUMENT-NUMBER: 20040169513
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040169513 A1

TITLE: Method of and device for the compensation of variations of the main magnetic field during magnetic resonance imaging

PUBLICATION-DATE: September 2, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ham, Cornelis L. G.	Eindhoven		NL	
Mulder, Gerardus B.J.	Eindhoven		NL	

US-CL-CURRENT: 324/315; 324/313

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 2. Document ID: US 20040066194 A1

L11: Entry 2 of 17 File: PGPB Apr 8, 2004

PGPUB-DOCUMENT-NUMBER: 20040066194
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040066194 A1

TITLE: Magnetic field generating assembly and method

PUBLICATION-DATE: April 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Slade, Robert Andrew	Oxon		GB	
Hawkes, Robert Carter	Cambridge		GB	
Lucas, Alun J.	Royston		GB	
McDougall, Ian Leitch	Oxon		GB	

US-CL-CURRENT: 324/318

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 3. Document ID: US 20030137299 A1

L11: Entry 3 of 17 File: PGPB Jul 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030137299
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030137299 A1

TITLE: Method of and device for the compensation of variations of the main magnetic field during magnetic resonance imaging

PUBLICATION-DATE: July 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ham, Cornelis L.G.	Eindhoven		NL	
Mulder, Geradus B. J.	Eindhoven		NL	

US-CL-CURRENT: 324/313; 324/315

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 4. Document ID: US 20030076281 A1

L11: Entry 4 of 17 File: PGPB Apr 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030076281
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030076281 A1

TITLE: DIFFUSE ILLUMINATION SYSTEMS AND METHODS

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
MORGAN, FREDERICK MARSHALL	QUINCY	MA	US	
LYS, IHOR	BOSTON	MA	US	

US-CL-CURRENT: 345/44

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 5. Document ID: US 20010051766 A1

L11: Entry 5 of 17 File: PGPB Dec 13, 2001

PGPUB-DOCUMENT-NUMBER: 20010051766
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010051766 A1

TITLE: Endoscopic smart probe and method

PUBLICATION-DATE: December 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Gazdzinski, Robert F.	San Diego	CA	US	

US-CL-CURRENT: 600/309; 128/903, 378/119, 600/300, 600/437, 600/562, 604/65, 606/1, 606/32, 607/92, 623/23.64

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 6. Document ID: US 6731113 B2

L11: Entry 6 of 17 File: USPT May 4, 2004

US-PAT-NO: 6731113
DOCUMENT-IDENTIFIER: US 6731113 B2

TITLE: Method of and device for the compensation of variations of the main magnetic field during magnetic resonance imaging

DATE-ISSUED: May 4, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ham; Cornelis L.G.	Eindhoven			NL
Mulder; Gerardus B.J.	Eindhoven			NL

US-CL-CURRENT: 324/313; 324/309, 324/315

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw D

☐ 7. Document ID: US 6566875 B1

L11: Entry 7 of 17 File: USPT May 20, 2003

US-PAT-NO: 6566875
DOCUMENT-IDENTIFIER: US 6566875 B1

TITLE: Portable hyperpolarized gas monitoring systems, computer program products, and related methods using NMR and/or MRI during transport

DATE-ISSUED: May 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hasson; Kenton C.	Durham	NC		
Wheeler; Bradley A.	Raleigh	NC		

US-CL-CURRENT: 324/309; 600/420, 604/181, 604/20, 62/3.1, 62/45.1, 62/49.1, 62/914

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw D

☐ 8. Document ID: US 6566873 B1

L11: Entry 8 of 17 File: USPT May 20, 2003

US-PAT-NO: 6566873
DOCUMENT-IDENTIFIER: US 6566873 B1

TITLE: Method of and apparatus for nuclear quadrupole resonance testing a sample

DATE-ISSUED: May 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Smith; John Alec Sydney	London			GB
Peirson; Neil Francis	Northampton			GB

US-CL-CURRENT: 324/300; 324/314

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw D

☐ 9. Document ID: US 6528954 B1

L11: Entry 9 of 17 File: USPT Mar 4, 2003

US-PAT-NO: 6528954
DOCUMENT-IDENTIFIER: US 6528954 B1
**** See image for Certificate of Correction ****

TITLE: Smart light bulb

DATE-ISSUED: March 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lys; Ihor	Boston	MA		
Mueller; George G.	Boston	MA		

US-CL-CURRENT: 315/291; 315/158

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw D

☐ 10. Document ID: US 6100688 A

L11: Entry 10 of 17 File: USPT Aug 8, 2000

US-PAT-NO: 6100688
DOCUMENT-IDENTIFIER: US 6100688 A

TITLE: Methods and apparatus for NQR testing

DATE-ISSUED: August 8, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Smith; John Alec Sydney	London			GB
Shaw; Julian David	Encinitas	CA		

US-CL-CURRENT: 324/300; 324/307, 324/322

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

☐ 11. Document ID: US 6013031 A

L11: Entry 11 of 17 File: USPT Jan 11, 2000

US-PAT-NO: 6013031
DOCUMENT-IDENTIFIER: US 6013031 A

TITLE: Methods and devices for improving ultrasonic measurements using anatomic landmarks and soft tissue correction

DATE-ISSUED: January 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mendlein; John D.	Encinitas	CA	92024	
Lang; Philipp	San Francisco	CA	94122	

US-CL-CURRENT: 600/442; 600/443, 600/449

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

☐ 12. Document ID: US 5814989 A

L11: Entry 12 of 17 File: USPT Sep 29, 1998

US-PAT-NO: 5814989
DOCUMENT-IDENTIFIER: US 5814989 A

TITLE: Methods and apparatus for NQR testing

DATE-ISSUED: September 29, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Smith; John Alec Syndney	London			GB2
Shaw; Julian David	Encinitas	CA		
Blanz; Martin	Culham			GB2

US-CL-CURRENT: 324/300; 324/307

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

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☐ 13. Document ID: US 5427102 A

L11: Entry 13 of 17 File: USPT Jun 27, 1995

US-PAT-NO: 5427102
DOCUMENT-IDENTIFIER: US 5427102 A

TITLE: Active noise cancellation apparatus in MRI apparatus

DATE-ISSUED: June 27, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shimode; Shin'ichi	Ibaraki			JP
Inouye; Hiroshi	Ibaraki			JP
Saho; Norihide	Tsuchiura			JP
Okabe; Shinya	Shimizu			JP
Otsuka; Masayuki	Katsuta			JP
Iwase; Yukiji	Ushiku			JP
Yamamoto; Etsuji	Akishima			JP
Shiono; Hidemi	Akigawa			JP
Takiguchi; Kenji	Kodaira			JP

US-CL-CURRENT: 600/410; 128/925, 324/318, 381/71.9

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

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☐ 14. Document ID: US 5020411 A

L11: Entry 14 of 17 File: USPT Jun 4, 1991

US-PAT-NO: 5020411
DOCUMENT-IDENTIFIER: US 5020411 A

TITLE: Mobile assault logistic kinetmatic engagement device

DATE-ISSUED: June 4, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rowan; Larry	Culver	CA	90230	

US-CL-CURRENT: 89/1.11; 376/319, 60/203.1, 89/8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. D

☐ 15. Document ID: US 4944211 A

L11: Entry 15 of 17 File: USPT Jul 31, 1990

US-PAT-NO: 4944211
DOCUMENT-IDENTIFIER: US 4944211 A

TITLE: Mass action driver device

DATE-ISSUED: July 31, 1990

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rowan; Larry	Culver City	CA	90230	
Rosenberg; Larry	Culver City	CA	90230	

US-CL-CURRENT: 89/8; 376/107

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. D

☐ 16. Document ID: US 3077984 A

L11: Entry 16 of 17 File: USOC Feb 19, 1963

US-PAT-NO: 3077984
DOCUMENT-IDENTIFIER: US 3077984 A

TITLE: OCR SCANNED DOCUMENT

DATE-ISSUED: February 19, 1963

INVENTOR-NAME: Name not available

US-CL-CURRENT: 209/569; 707/7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. D

☐ 17. Document ID: US 2301184 A

L11: Entry 17 of 17 File: USOC Nov 10, 1942

US-PAT-NO: 2301184
DOCUMENT-IDENTIFIER: US 2301184 A

TITLE: Electrical clarinet

DATE-ISSUED: November 10, 1942

INVENTOR-NAME: ARNOLD LEO F J

US-CL-CURRENT: 84/742; 984/344, 984/DIG.1

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Term	Documents
PRESSURE	4115702
PRESSURES	519854
ATM	119139
ATMS	9968
ATMOSPHER$4	0
ATMOSPHER	5389
ATMOSPHERA	52
ATMOSPHERAC	4
ATMOSPHERAL	1
ATMOSPHERAND	4
ATMOSPHERAS	1
(L10 AND (PRESSURE OR "ATM" OR ATMOSPHER$4)).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	17

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L11: Entry 7 of 17 File: USPT May 20, 2003

DOCUMENT-IDENTIFIER: US 6566875 B1
TITLE: Portable hyperpolarized gas monitoring systems, computer program products, and related methods using NMR and/or MRI during transport

Abstract Text (1):
A system, method, and computer program products and associated apparatus, to monitor and determine the polarization level of a quantity of hyperpolarized gas during transport. A portable device is configured to transmit an excitation pulse and analyze a response signal in transit to provide a polarization level corresponding to the hyperpolarized gas. Preferably, the monitoring system can provide magnetic field fluctuation feedback to the transport unit and adjust operating current to a solenoid. The system also can compensate for NMR frequency shifts that may appear in the measured response signal to provide a more accurate polarization level or "real" T.sub.1 for the hyperpolarized gas.

Brief Summary Text (2):
The present invention relates generally to systems of determining or monitoring the condition of hyperpolarized gas, such as monitoring the polarization level of the hyperpolarized gas during transport. The hyperpolarized gases are particularly suitable for MR imaging and spectroscopy applications.

Brief Summary Text (4):
Inert gas imaging ("IGI") using hyperpolarized noble gases is a promising recent advance in Magnetic Resonance Imaging (MRI) and MR spectroscopic technologies. Conventionally, MRI has been used to produce images by exciting the nuclei of hydrogen molecules (present in water protons) in the human body. However, it has recently been discovered that polarized noble gases can produce improved images of certain areas and regions of the body, which have heretofore produced less than satisfactory images in this modality. Polarized Helium-3 (".sup.3 He") and Xenon-129 (".sup.129 Xe") have been found to be particularly suited for this purpose. Unfortunately, as will be discussed further below, the polarized state of the gases are sensitive to handling and environmental conditions and can, undesirably, decay from the polarized state relatively quickly.

Brief Summary Text (5):
Various methods may be used to artificially enhance the polarization of certain noble gas nuclei (such as .sup.129 Xe or .sup.3 He) over the natural or equilibrium levels, i.e., the Boltzmann polarization. Such an increase is desirable because it enhances and increases the MRI signal intensity, allowing physicians to obtain better images of the substance in the body. See U.S. Pat. No. 5,545,396 to Albert et al., the disclosure of which is hereby incorporated by reference as if recited in full herein.

Brief Summary Text (6):
A "T.sub.1 " decay constant associated with the hyperpolarized gas's longitudinal relaxation time is often used to characterize the length of time it takes a gas sample to depolarize in a given situation. The handling of the hyperpolarized gas is critical because of the sensitivity of the hyperpolarized state to environmental and handling factors and thus the potential for undesirable decay of the gas from its hyperpolarized state prior to the planned end use, e.g., delivery to a patient

for imaging. Processing, transporting, and storing the hyperpolarized gases--as well as delivering the gas to the patient or end user--can expose the hyperpolarized gases to various relaxation mechanisms such as magnetic field gradients, surface-induced relaxation, hyperpolarized gas atom interactions with other nuclei, paramagnetic impurities, and the like.

Brief Summary Text (10):
It is therefore an object of the present invention to provide a portable monitoring system which can determine the polarization level of the hyperpolarized gas (and/or hyperpolarized gas products) during transport.

Brief Summary Text (11):
It is another object of the present invention to provide a monitoring system that can automatically adjust a magnetic holding field to a predetermined or optimal value. By so doing, the resonant frequency of the gas can be shifted above that of potentially substantially depolarizing environmental conditions during movement of the hyperpolarized gas products from a production site to a remote use site, thus increasing the usable lifespan of the hyperpolarized gas products.

Brief Summary Text (13):
It is a further object of the present invention to provide a portable system which can provide information to a user and which allows user input to react to the information about gas-related parameters, thereby allowing a user to be alerted to and thus take action to reduce the likelihood of any introduction of substantially depolarizing factors onto the hyperpolarized gases (such as unprotected exposure to stray magnetic gradients).

Brief Summary Text (14):
It is another object of the present invention to provide a method for determining the polarization level of a quantity of hyperpolarized gas at successive intervals in time to determine the effectiveness of the hyperpolarized product and to determine the overall polarization decay rate.

Brief Summary Text (15):
It is yet another object of the present invention to provide a method of reliably identifying gas polarization values corresponding to a quantity of hyperpolarized gas during transport and/or at a destination site, particularly in the presence of stray magnetic fields.

Brief Summary Text (16):
It is an additional object of the present invention to provide a method for determining the polarization of the gas in a manner which accounts for NMR coil resonance to more accurately measure the polarization level of the gas.

Brief Summary Text (17):
These and other objects of the present invention are provided by a portable monitoring system for determining the polarization of hyperpolarized gas in transit. The method includes transporting a quantity of hyperpolarized gas from a first site to a second site and intermittently transmitting a predetermined excitation pulse to the quantity of hyperpolarized gas during the transporting step. An NMR signal corresponding to the response of the hyperpolarized gas to the excitation pulse is received. The magnitude of this signal is then multiplied by a calibration factor and the level of polarization of the hyperpolarized gas is determined. The method also preferably includes the step of selecting the excitation pulse such that a plurality of transmitted pulses are substantially non-depolarizing to the quantity of hyperpolarized gas. In a preferred embodiment, the received signal is analyzed and a frequency-dependent correction factor is applied to adjust the signal polarization value to compensate for any externally-induced frequency shift that may appear in the measured signal value.

Brief Summary Text (18):
Another aspect of the present invention is directed toward a portable monitoring system for determining the polarization level of a quantity of hyperpolarized gas product. The system includes positioning a NMR coil proximate to a quantity of hyperpolarized gas product packaged for transport from a first site to a second site and transmitting an excitation pulse to the NMR coil to, in turn, excite the hyperpolarized gas product. A signal corresponding to the response of the hyperpolarized gas product to the excitation pulse is received by the NMR coil and the response signal is analyzed to determine the polarization level of the hyperpolarized gas product during transport. The system also includes an adjustment means for compensating the magnetic field strength associated with a magnetic holding field that is positioned such that it is operably associated with the quantity of hyperpolarized gas during transport. In a preferred embodiment, the adjustment means can be used to alter the magnetic field so that a transmit and receive frequency used for monitoring the gas corresponds to an optimal value associated with the NMR coil resonance.

Brief Summary Text (19):
In a preferred embodiment, the hyperpolarized gas product is held within a transport unit having a cylindrically or longitudinally extending solenoid coil used to generate a magnetic holding field for the hyperpolarized gas. Also preferably, the portable monitoring system includes a current input adjustment means which is configured to compensate for detected magnetic holding field strength fluctuations (such as to change or increase the current into the solenoid used to generate a magnetic holding field for the hyperpolarized gas or product held in a chamber therewithin to optimize the field strength of the magnetic holding field).

Brief Summary Text (20):
An additional aspect of the present invention is a computer program product for monitoring and/or determining the polarization level of a hyperpolarized gas product. The computer program product comprises a computer readable storage medium having computer readable program code means embodied in said medium, the computer readable program code means comprising a computer readable program code means for selecting an excitation pulse. The program also includes a computer readable program code means for transmitting the selected excitation pulse to a quantity of hyperpolarized noble gas product and a computer readable program code means for analyzing a signal associated with the response of the hyperpolarized noble gas product to the excitation pulse. The program further includes a computer readable program code means for compensating the response signal such that it more accurately corresponds to the hyperpolarization level of the gas and a computer readable program code means for determining the polarization level of the hyperpolarized gas.

Brief Summary Text (21):
In a preferred embodiment, the computer program product also comprises a computer readable program code means for generating a correction factor table corresponding to a Fourier transform of an NMR coil response and a computer readable program code means for applying a correction factor corresponding to the frequency of a measured response to produce a corrected value.

Brief Summary Text (22):
Another aspect of the present invention is directed to a portable transport unit for hyperpolarized gas in combination with monitoring apparatus. The apparatus comprises a portable transport unit configured to hold a quantity of hyperpolarized gas therein and a NMR coil configured and sized to be positioned in a portable transport unit such that it is proximate to a quantity of hyperpolarized gas product. The apparatus also includes a pulse generator for generating an excitation pulse. The apparatus additionally includes transmit and receive means operably associated with the pulse generator and the NMR coil. The transmit means transmits

the excitation pulse to the hyperpolarized gas via the coil and the receive means receives a signal corresponding to the response of the hyperpolarized gas to the transmitted excitation pulse. A signal analyzer is operably associated with the receive means. The analyzer includes a computer readable program code means for determining the polarization level of the hyperpolarized gas during transport.

Brief Summary Text (23):
In a preferred embodiment, the combination monitoring system and portable transport unit comprises a solenoid configured to generate an adjustable electromagnetic holding field proximate to the quantity of hyperpolarized gas and the adjustability of the holding field corresponds to the current input to the solenoid. The present invention is advantageous because the monitoring system is portable and readily engaged to a transport device. Further, the portable monitoring system can correct for environmentally-induced signal shift and yield a more accurate T.sub.1 value for the hyperpolarized gas. In addition, the portable monitoring system can provide feedback about ambient conditions or about temporal magnetic holding field variations and allow for the adjustment of same to minimize the depolarizing effects attributed to stray magnetic fields, especially deleterious oscillating fields which can easily dominate other relaxation mechanisms. Preferably, the monitoring system can automatically adjust the current provided to the solenoid that generates the magnetic holding field. The automatic adjustment (and/or with user input) can shift the strength of the magnetic holding field according to external or internal (circuitry) parameters; for example, to shift the resonance frequency of the hyperpolarized gas away from an external deleterious event (such as a proximate static magnetic field). In addition or alternatively, the monitoring system can detect field drift due to temperature-induced resistance variation in the coil(s) and adjust the current input to the solenoid to maintain the desired field strength. Further, the monitoring system can verify the level of polarization at the destination site providing an easy inspection device for receiving inspection purposes/delivery verification. Indeed, the monitoring system is preferably configured such that the hyperpolarized gas can be analyzed within the transport unit such that the hyperpolarized gas can be checked both during transit and at the end use site without removing the relatively fragile gas container from the transport unit. Advantageously, the monitoring system can verify via an on-board portable non-destructive test (NDT) method, that the transported product meets the applicable polarization level standard at an incoming/receiving inspection dock and/or immediately prior to use.

Drawing Description Text (6):
FIG. 4 is a flow chart of a system for monitoring or determining (in transit) the polarization level of a quantity of hyperpolarized gas.

Drawing Description Text (8):
FIG. 6 is a flow chart of a system for determining the polarization level of a quantity of hyperpolarized gas by using a correction factor according to a preferred embodiment of the present invention.

Drawing Description Text (9):
FIG. 7 is a graphical representation of a frequency corrected value (upper line--squares) versus the measured, uncorrected signal values (lower line--diamond shapes).

Drawing Description Text (10):
FIG. 8 is a graphic user interface of a preferred set of pulse parameters for determining coil resonance to be used with the monitoring system according to a preferred embodiment of the present invention.

Drawing Description Text (12):
FIG. 10 illustrates a "look-up" correction chart for compensating a received signal according to the present invention.

Detailed Description Text (6):
Various techniques have been employed to polarize, accumulate and capture polarized gases. For example, U.S. Pat. No. 5,642,625 to Cates et al. describes a high volume hyperpolarizer for spin-polarized noble gas and U.S. Pat. No. 5,809,801 to Cates et al. describes a cryogenic accumulator for spin-polarized .sup.129 Xe. The disclosures of these patents are hereby incorporated herein by reference as if recited in full herein. As used herein, the terms "hyperpolarize" and "polarize" are used interchangeably and mean to artificially enhance the polarization of certain noble gas nuclei over the natural or equilibrium levels. Such an increase is desirable because it allows stronger imaging signals corresponding to better MRI images of the substance in a targeted area of the body. As is known by those of skill in the art, hyperpolarization can be induced by spin-exchange with an optically pumped alkali-metal vapor or alternatively by metastability exchange. See U.S. Pat. No. 5,545,396 to Albert et al. The alkali metals capable of acting as spin exchange partners in optically pumped systems include any of the alkali metals. Preferred alkali metals for this hyperpolarization technique include Sodium-23, Potassium-39, Rubidium-85, Rubidium-87, and Cesium-133.

Detailed Description Text (7):
Alternatively, the noble gas may be hyperpolarized using metastability exchange. (,See e.g., Schearer, L. D., Phys Rev, 180:83 (1969); Laloe, F., Nacher, P. J., Leduc, M., and Schearer L. D., AIP ConfProx #131 (Workshop on Polarized .sup.3 He Beams and Targets) (1984)). The technique of metastability exchange involves direct optical pumping of, for example, .sup.3 He without the need for an alkali metal intermediary. Since this process works best at low pressures (0-10 Torr), a compressor is typically used to compress the .sup.3 He after the hyperpolarization step.

Detailed Description Text (8):
Regardless of the hyperpolarization method used, once the active mechanism is no longer in effect, the polarization of the gas will inevitably decay toward its thermal equilibrium value, which is essentially zero. The present invention is configured to work with any hyperpolarization technique and is not limited to working with any one machine, method, or gas.

Detailed Description Text (13):
As will be appreciated by those skilled in the art, these relaxation mechanisms can themselves be time-dependent. For example, transporting a hyperpolarized gas or hyperpolarized product can potentially and/or unpredictably expose the sensitive hyperpolarized gas or product to EMI or gradient relaxation mechanisms, each of which can be particularly destructive to the sensitive polarized state of the gas. The instant invention recognizes such potential and now provides a reliable and portable polarization monitoring system which can generate a rapid (substantially instantaneous) quantitative measurement of the viability of the hyperpolarized gas undergoing evaluation. In addition, the portable monitoring system of the instant invention can be used to minimize the effects of certain external potentially deleterious conditions.

Detailed Description Text (15):
The relaxation mechanism expressed by the term (1/T.sub.1).sub.EMI is the relaxation induced by time-dependent electromagnetic fields. Indeed, EMI can potentially destroy the hyperpolarized state of the gas (EMI is particularly problematic if coherent at the magnetic resonance frequency). Unfortunately, EMI can be generated by relatively common sources. For example, EMI is typically generated from a vehicle's engine, high voltage lines, power stations and other current carrying entities. As such, transport away from the hyperpolarized gas production site can expose the hyperpolarized gas to these undesirable relaxation sources that, in turn, can dramatically reduce the polarization lifetime of the transported gas.

Detailed Description Text (16):
Fluctuating fields are particularly deleterious if they are coherent at the magnetic resonance frequency. In a severe case scenario of a highly coherent oscillating field, the relaxation rate can be assumed to be comparable to the Rabi frequency:

Detailed Description Text (20):
Magnetic Field Gradients

Detailed Description Text (21):
Magnetic gradient relaxation ((1/T.sub.1).sub.Gradient) involves the relaxation attributed to the exposure of the hyperpolarized noble gases to inhomogeneous static magnetic fields. Generally stated, as the polarized gas atoms diffuse or move through an inhomogeneous magnetic field, they experience a time-dependent field, which can introduce depolarizing activity onto the hyperpolarized atoms.

Detailed Description Text (22):
As will be appreciated by those of skill in the art, during transport, it is desirable to avoid inhomogeneous magnetic fields, i.e., to avoid nearby ferromagnetic and paramagnetic objects. For example, it is desired to maximize the spatial distance between the hyperpolarized gas and objects like car frames and axles, which can have static spatial gradients of varying strength.

Detailed Description Text (24):
The present invention recognizes that unless special precautions are taken, relaxation due to stray magnetic fields (static and/or EMI) can dominate all other relaxation mechanisms. As discussed above, both gradients in the static field and (low frequency) oscillating magnetic fields experienced by the hyperpolarized gas can cause significant relaxation. The stray magnetic fields can be especially problematic when shipping a polarized product from one site to another. Advantageously, the portable monitoring system of the instant invention is preferably configured to engage with a transport unit which generates an applied magnetic holding field "B.sub.H " to substantially protect the hyperpolarized gas from potentially depolarizing effects attributed to one or more of the EMI and gradient fields during transport. The transport unit win be discussed further below.

Detailed Description Text (25):
In a preferred embodiment, as schematically illustrated in FIG. 1, the portable monitoring system 100 of the present invention can engage with a shielded and portable or storable container or transport unit 10 (the transport unit components are illustrated as outer dotted line) to provide feedback and allow a user (preferably automatically or semi-automatically) information relevant to the status of the polarized gas or related operational details of the transport unit 10. For example, the monitoring system 100 is preferably configured to determine when or if an adjustment is needed to optimize an applied magnetic holding field ("B.sub.H ") 300. Referring to FIG. 2, when used with the transport unit 10 which comprises a solenoid 20 to generate the magnetic holding field 300, the monitoring system 100 is preferably configured to increase the current input to the solenoid 20 to raise the Larmor frequency of the hyperpolarized gas above a region of noise (1/f), i.e. the region where the intensity of ambient electromagnetic noise is typically high.

Detailed Description Text (27):
Referring again to FIG. 1, generally described, the monitoring system 100 of the instant invention determines the polarization level of the polarized gas 200 (or polarized gas based product) during transport. Preferably, the monitoring system 100 also activates, directs, adjusts, compensates for and supplies the power or input needed for the magnetic holding field (shown by dotted line as inner box 300) operably associated with a hyperpolarized gas 200 (shown enclosed by box 220). As

noted above, the magnetic holding field 300 is selected and positioned proximate to the polarized gas 200 such that it reduces the hyperpolarized gas's 200 sensitivity to potentially depolarizing sources, such as static and/or oscillating magnetic field gradients. By applying a magnetic holding field (preferably an adjustable static field) which is sufficiently homogeneous, the applied field substantially supersedes ambient fields, which reduces gradient-induced relaxation during transport. Additionally, in operation, depolarizing events such as external EMI or oscillating fields are preferably (substantially) blocked by adjusting the field strength of the magnetic holding field (B.sub.H) 300 proximate to the gas 200 so that the gas-attendant magnetic field (B.sub.0) is increased (to increase the resonant frequency of the hyperpolarized gas). Application of a homogeneous magnetic holding field 300 proximate to the hyperpolarized gas 200 can help minimize the gas depolarization by pushing the resonant frequency of the gas outside the bandwidth of common AC fields. It is preferred that the resonant frequency of the hyperpolarized gas be raised such that it is above about 10 kHz, and more preferably the resonant frequency be raised such that it is between about 20-30 kHz.

Detailed Description Text (28):
Stated differently, it is preferred that the magnetic holding field 300 has a field strength in the range of about 2 gauss-35 gauss. It is more preferred that for .sup.129 Xe, the magnetic holding field is preferably at least about 20 gauss; and for .sup.3 He, the magnetic holding field is preferably at least about 7 Gauss.

Detailed Description Text (30):
As schematically shown in FIG. 1, the portable monitoring system 100 of the present invention preferably includes a signal analyzer 110, a pulse generator 115, a transmit/receive element preferably a NMR coil) 150, a power source 120 (preferably a DC battery for easy transport), and a power monitoring circuit 325. The portable monitoring system 100 also includes an input pulse transmitter 111, and a signal receiver 112 (which can be the same line) and which are operably associated with the signal analyzer 110 and the NMR coil 150 (positioned adjacent the hyperpolarized gas sample 200). As discussed above, in a preferred embodiment, the portable monitoring system 100 is configured to engage with a portable transport unit 10. As such, certain of the operational circuitry is preferably configured to engage with the transport unit 10 such that the portable monitoring system 100 is dominant and can direct the power input into the transport unit 10.

Detailed Description Text (31):
Preferably, as shown in FIG. 2, the NMR coil element 150 is a NMR surface excitation coil 75 which is positioned to contact the container 30 holding the hyperpolarized gas (or hyperpolarized gas based product) which is preferably held within a magnetic holding field B.sub.H 300. As such, the magnetic holding field 300 is preferably generated by a magnetic field source such as a set of permanent magnets or a solenoid, such as internal solenoid 20, positioned in the transport unit 10 itself and is configured to provide a homogeneous holding region for the quantity of gas held therein. It is also preferred that the portable monitoring system 100 is configured to engage with a transport unit 10 with an internal solenoid 20 in a manner which allows the system 100 to control or adjust the power output level of the solenoid 20 which generates the magnetic holding field 300. Optionally, as shown in FIG. 1, the portable monitoring system 100 can also include a display 160 for visually indicating various desired parameters such as the polarization level of the gas, the elapsed transit time (age of the gas), the field strength of the magnetic holding field, and the like.

Detailed Description Text (32):
Preferably, as shown in FIG. 1, the portable monitoring system 100 also includes a user input 140 for allowing a user to adjust various parameters (power adjustment, pulse characteristics, field strength, on/off switch, and the like) in response to

external conditions. In a preferred embodiment, the portable monitoring system's 100 power monitoring circuit 325 is electrically connected to the power source 120 and an externally accessible user input 140. The user input 140 can allow a user to change certain operational parameters. For example, the user input 140 can be used to allow a user to set desired frequency, current, or other parameters associated with the signal analyzer 110, pulse generator 115, power source 120, or power monitoring circuit 325. Generally described, in operation, a selected RF pulse (of predetermined frequency, amplitude, and duration) is transmitted from the pulse generator 115 to the NMR surface coil 150.

Detailed Description Text (33):
The signal analyzer 110 is preferably operably associated with a portable laptop computer (500, FIG. 5) but can also be operative with other electronic and/or hardware equipment. The power monitoring circuit 325 can be configured as described for the transport unit 10 below. Generally summarized, the power monitoring circuit 325 is preferably configured to automatically switch the power source 120 from a battery to an external source upon electrical engagement with same to preserve the charged state of the battery (and can include a battery charger to recharge the internal battery during the external powering). Further, the portable monitoring system 100 also preferably includes an alarm 145 to alert the user to potential problems such as external environmental conditions, low magnetic holding field strength, low battery power, low polarization levels, current fluctuation in the solenoid 20, and the like.

Detailed Description Text (34):
Generally described, as diagrammatically shown in FIG. 4, in operation, a monitoring method is used to monitor the polarization of the hyperpolarized gas (Block 399). At least once, a NMR coil resonance frequency (Block 425) is determined. This value should be stable during most transports, however, the coil resonance may shift over long periods of use or after re-assembly, and, as such, a new NMR coil resonance value is preferably established prior to each new transport.

Detailed Description Text (35):
The pulse generator 115 transmits a (selected) excitation pulse to the surface coil 150 (FIG. 1) (Block 400, FIG. 4)). The transmitted excitation pulse locally excites a small fraction of the hyperpolarized gas sample or hyperpolarized gas based product 200 (FIG. 1) (Block 410, FIG. 4). The hyperpolarized gas 200 responds to the excitation pulse, inducing a response signal back to the signal analyzer 110. Thus, a signal is received corresponding to the response of the gas to the excitation pulse (Block 420). The received signal is analyzed (Block 430) to determine the polarization of the hyperpolarized gas (Block 440).

Detailed Description Text (36):
Preferably, the analyzing step includes the step of determining the field strength associated with the hyperpolarized gas (Block 455). Also preferably, this step also includes the step of determining if there are any detectable magnetic field fluctuations in the holding field (to optimize the desired holding field) (Block 458).

Detailed Description Text (37):
As shown in FIG. 4, the analyzing step also preferably includes compensating the received gas monitoring signal (Block 435). Preferably, the compensating step includes analyzing the data corresponding to the received signal to compensate for predetermined events such as frequency drift or shift (such as by applying a correction factor) (Block 457) if the presence of a frequency offset in the received signal is determined (Block 456). Alternatively or additionally, the received signal can be analyzed to determine if the magnetic holding field strength needs to be adjusted to provide an optimal receive frequency. If this is needed, the method can adjust the electric current introduced into the solenoid to adjust

the field strength (Block 460).

Detailed Description Text (38):
This type of analysis (and compensation and/or adjustment) can provide a more reliable value(s) for the response signal, and therefore, a more representative polarization level of the hyperpolarized gas/hyperpolarized gas-based product. Thus, the monitoring system of the present invention preferably compensates the field strength associated with the measured "received signal data" and/or corrects the received signal to correspond to the selected frequency. As noted above, the frequency-dependent correction value corresponding to the NMR coil resonance can be used to provide a more accurate polarization value.

Detailed Description Text (39):
In any event, the polarization value of the gas is determined (Block 440) based on the analyzed signal. The value can then be displayed such that it is readily externally visually discerned (Block 450). Indeed, the system can analyze the received signal to alert to transport equipment problem conditions as well as to (semi-) continuously monitor the polarization level of the gas. Preferably, the monitoring system can also act to optimize the power input to the solenoid to provide the desired (constant) holding field strength. Further, the system can be programmed to "automatically" adjust the field strength to obtain the desired receive signal frequency. Advantageously, this method can be intermittently repeated (multiple times) during transport as well as when in a stationary mode to instantaneously provide a contemporaneous and reliable measure of gas polarization.

Detailed Description Text (40):
Preferably, the excitation pulse is a RF pulse having a selected pulse time and frequency that corresponds to the strength of the magnetic field and the particular hyperpolarized gas. The frequency is preferably determined by the NMR coil analysis, discussed further below. The RF pulse generates an oscillating magnetic field which misaligns a small fraction of the hyperpolarized gas (i.e., .sup.3 He or .sup.129 Xe) nuclei from their static magnetic field alignment position. The misaligned nuclei start precessing at their associated Larmour frequency (corresponding to pulse frequency). The precessing spins induce a voltage in the NMR coil 75 (FIG. 2) (also schematically shown in FIG. 1 as element 150) which can be processed to represent a data signal. The voltage is received back (typically amplified) at the computer and the signal typically fits an exponentially decaying sinusoid pattern. The initial peak-to-peak voltage of this signal is directly proportional to polarization (using a known calibration constant). The computer can then calculate the polarization level, and generate predicted shelf life (i.e., a "use by" time/date) corresponding to the decay rate and the initial polarization value, or the current polarization (corrected) measurement value. Advantageously, such a portable monitoring system can be configured to continuously monitor the hyperpolarized product right up to delivery to a patient thereby insuring only sufficiently active product is introduced to a patient via inhalation or injection or the like.

Detailed Description Text (41):
In FIG. 6, a preferred NMR coil 75 optimal frequency routine is illustrated and is preferably used in the monitoring system 100 according to the present invention. As shown, the monitoring system 100 can compensate for a frequency shift that may appear in the measured response signal data to provide a more accurate or "real" measure of T.sub.1 and polarization level for the hyperpolarized gas. This can be helpful in transport units which include permanent magnet holding field sources, as well as solenoid-generated magnetic fields. To obtain a T.sub.1 value for the hyperpolarized gas, several temporally separated measurements of the polarization level of the gas are obtained according to the monitoring system described above. A single parameter representing the instantaneous polarization level is extracted from each measurement. These values are fit to a decaying exponential to determine

the corresponding T.sub.1.

Detailed Description Text (42):
Generally stated, the response received back at the signal analyzer 110 corresponding to the transmitted excitation pulse varies depending on the magnetic (holding) field strength. Further, each NMR coil 75 may have a different resonant frequency. Thus, in order to obtain a more accurate determination of the polarization level of the gas, the coil data, i.e., the resonance of the NMR coil 75, is used to define an "optimal" transmit and receive frequency for the monitoring of hyperpolarized gas. Matching the response signal's frequency to the NMR coil's 75 resonant frequency yields a more accurate and substantially contemporaneous representation of the actual status of the polarization of the gas at that time. Preferably, as will be discussed further below, the received response signal frequency is monitored to assure that it substantially corresponds to the NMR coil 75 established optimal frequency as is discussed under the NMR coil optimal frequency section below.

Detailed Description Text (43):
FIG. 7 illustrates via the lower line, a measured (uncorrected) T.sub.1 of .sup.3 He in a sealed chamber held within a solenoid 20 which generates a magnetic holding field. The received signal data is monitored and corrected to force the received signal data to substantially emulate the values associated with the selected optimal transmit frequency and thus obtain a more accurate or "frequency corrected" signal value (upper line) for polarization measurement. The corrected signal (upper line) can be provided by applying a correction factor to the signal as discussed in the flow chart of FIG. 6 and/or by adjusting the field strength of the magnetic holding field (when adjustable) to shift or correct the frequency of the received signal once frequency drift is detected. Once the strength of the magnetic field is shifted to force the resonant frequency of the hyperpolarized product to reflect the resonant frequency of the NMR coil, subsequent measurements will be optimized. Thus, in operation, a sample data point (or points) at a first receive frequency will be monitored and if offset from predicted values, alert the monitoring system to alter the current to the solenoid to make the subsequent points correct, i.e., shift the frequency to a second frequency to match the optimal transmit frequency. The detected offset or shifted frequency data points can then be ignored in the polarization measurement or corrected by applying the appropriate correction factor. As shown, after the initial data points (fifth), the magnetic field strength changed, causing the uncorrected polarization measurements (lower line) to drop significantly. However, as also shown, the corrected data (upper line) follows the expected exponential decay curve and experiences no corresponding drop despite the field fluctuation, thus providing a more accurate measure of polarization and T.sub.1.

Detailed Description Text (44):
Referring again to FIG. 6, in a preferred embodiment, the received signal is analyzed to correct for the frequency dependent signal information. As shown in Block 600, data associated with the coil is obtained. That is, a NMR excitation pulse is transmitted to the coil and a coil-ring down response is obtained using parameters such as those shown in FIG. 8. A Fourier transform is generated from the coil response.(Block 610). Additional discussion of a suitable coil resonance analysis is described below. After analyzing the coil response, the coil response analysis can be fed into a computer based "look-up" table or sub-routine which can be used to help establish a more accurate polarization based signal value as described more below. FIG. 10 illustrates a sample of a preferred correction factor "look-up" chart for an optimal frequency of 23.10 kHz. As shown in FIG. 10, the look-up chart provides a correction factor in millivolts to be applied to the received signal data based on the actual received signal frequency value (first column). Referring back to FIG. 6, as such, the coil response is used to create a "factor table" of normalized values based on ideal resonant frequency (Block 620). The NMR coil 75 will typically have a fixed response at a particular frequency and

temperature, but may have an associated frequency shift over time (which can be attributed to various factors such as temperature-induced resistance variation in the coil wire, use of different cables). As such, it is preferred that a coil response analysis be performed prior to each transport unit use. Lookup tables are very useful when the magnetic field is not easily adjustable, such as for permanent magnet arrangement field sources, but of course, can also be helpful for other magnetic field sources such as the solenoid described herein.

Detailed Description Text (45):
In any event, a T.sub.1 study is commenced (Block 630) and an excitation pulse is transmitted to the gas. The NMR signal is sampled (Block 640) for a desired number of samples (Blocks 641, 642 and 645), each of the samples being time related data points The received signal is monitored, i.e., a Fourier transform including data points associated with each time-related but sequential data point associated with each different polarization sample measure is generated (Block 650) The fundamental frequency of the response signal (measured) is compared to the factor table values and the response signal is corrected for frequency drift (Block 660). The corrected value is fit to correspond to a decaying exponential line (Block 670). The T.sub.1 value of the hyperpolarized gas is extracted by fitting the data sample "n" corrected values (obtained in Block 670) to an exponential decaying line (Block 680). The corrected polarization value can then be displayed (Block 690).

Detailed Description Text (47):
The present invention configures the portable monitoring system 100 such that the polarization measurement is substantially non-destructive to the hyperpolarized state of the gas. More particularly, the excitation pulse of the instant invention is selected such that it can reliably determine the level of polarization while depolarizing the gas an insignificant amount.

Detailed Description Text (49):
Preferably, as shown in FIG. 9, the monitoring system 100 is configured to engage with a portable transport unit such that it electrically connects to the power monitoring circuit 325 which is integrally mounted within or on the transport unit 10 itself. In this embodiment, it is preferred that the monitoring system 100 be configured to provide the dominant control system so as to direct the excitation pulse as well as the holding field current adjustment. FIG. 3A illustrates a preferred embodiment of operating circuitry 50 for the transport unit 10. The transport unit 10 includes a power monitoring and switching circuit 325, an on/off power switch 361 (to disengage the solenoid 20) and a current adjustment 380 to adjust current supplied to the solenoid 20). Advantageously, the power monitoring circuitry 325 is preferably configured to automatically switch between the different power sources (40, 340) without interruption of the current to either the-operating circuitry 50 or the solenoid 20. Preferably, the power monitoring and switching circuit 325 manages the power supply such that the transport unit 10 is powered from the internal power source 40 (battery) only when needed. For example, when the transport unit 10 is not easily connected to an external power source 340, the power monitoring circuit 325 engages the battery 40 to supply the power to the transport unit 10. Preferably, the power monitoring circuit 325 then disengages the battery 40 when the transport unit 10 is connected to a viable external power source 340 (such as a wall or vehicle power outlet). In a preferred embodiment, as shown in FIG. 3B, the power monitoring circuit 325 also can include a recharging circuit 348 which allows the internal battery to be recharged when the transporter is powered from an external supply 340.

Detailed Description Text (50):
Of course, as shown in FIG. 3A, the operating circuit 50 can also include other components and circuits such as a battery monitor 326 and an audible and/or visual alarm 327 to indicate when the battery 40 is low, Preferably, the transport unit 10 includes a current readout 351 (FIG. 3B) associated with the power monitoring circuit 325. As shown in FIG. 5, the current readout is an LCD display 351 which

will allow a custodian to monitor the input current to the solenoid while adjusting it via the current control knob 180 (also shown in FIG. 2). Also as shown in FIG. 3A, the operating circuitry 50 preferably includes a current adjustment means 380 for increasing or decreasing the current delivered to the solenoid 20. As discussed above, the adjustable current means preferably is adjustable to supply between about 100 mA to about 2.0A.

Detailed Description Text (51):
The current adjustment 380 allows the operating circuit to change the current introduced to the solenoid 20 responsive to the needs of the transport unit. For example, the current can be adjusted to provide a custom holding field corresponding to the type of hyperpolarized gas being transported. Additionally, the current to the solenoid 20 can be adjusted to compensate for electronic or mechanical system variation (i.e., battery drainage, electronic drift, coil resistance variability due to temperature sensitivity) thereby maintaining the desired holding field strength.

Detailed Description Text (52):
As with all materials that contact, or are positioned near or proximate to the hyperpolarized gas, it is preferred that the operating circuitry 50 be devoid of magnetically active materials and components such as iron transformers. However, if such materials or components are used, then it is preferred that they be positioned a sufficient distance from the gas chamber 30 and the solenoid 20 so that they do not cause undue gradient relaxation. Further, it is preferred that temperature-sensitive diodes be removed from the operating circuit 50 in order to provide a reliable, consistent circuit which can tolerate broad temperature ranges (inside and outside). Of course the operating circuitry 50 may be present in hardware, software, or a combination of software and hardware.

Detailed Description Text (54):
Upon engagement to the transport unit 10, the signal analyzer 110 (FIG. 1) is operably configured to direct the transmit pulse and receive signals corresponding to the level of polarization in the hyperpolarized gas sample 200 being analyzed. The gas sample 200 is proximately positioned inside the magnetic holding field or shield means 300. As such, the monitoring system 100 is conveniently configured to monitor the polarization level of hyperpolarized gas before, during, or after transport (such as that contained in a gas chamber 30, FIG. 2). Advantageously, such a monitoring system 100 can be used both in transit and at a desired evaluation site. For example, when used with a transport unit such as that shown in FIGS. 2 and 5, at the end use site, prior to the release of the hyperpolarized gas 200 from the transport unit 10, the monitoring system 100 can determine a polarization level corresponding to the polarization level of the hyperpolarized gas in the transport unit 10 at that time and thus indicate to an end use site the viability of the gas prior to delivery to a patient or at a receiving station at the use site. This can confirm (reliably "inspect") the viable life of the polarized product and assure that the product meets purchase specification prior to acceptance at the use site.

Detailed Description Text (55):
As noted above, in a preferred embodiment, the polarization monitoring system can also be used with the transport unit 10 to evaluate the gas and/or magnetic holding field fluctuations during transport and can automatically (or with user input) adjust the current to compensate for detected fluctuations.

Detailed Description Text (56):
As shown in FIG. 2, the monitoring system includes a NMR signal means 75 proximately located adjacent the hyperpolarized gas. For example, as shown in FIG. 2, the signal means is a NMR surface coil 75 which is positioned such that it (securely or firmly) contacts the external wall of the storage chamber 30. The NMR coil 75 includes an input/output line such as unitary transmit/receive signal line

111 (112) which is operably associated with a signal analyzer and/or pulse generator 110, 115 (FIG. 1) (and preferably operably associated with a portable computer device 500 (FIG. 5)). Preferably, the transport unit 10 includes a computer access port 300 which is operably associated with the operating circuitry 50 and the NMR coil 75 via the BNC NMR bulkhead 275. The NMR coil 75 can be used with the monitoring system 100 to evaluate the polarization level of the hyperpolarized gas in a substantially nondestructive test (NDT) technique.

Detailed Description Text (57):
As will be recognized by those of skill in the art, other calibration or hyperpolarization level determination methods can also be employed and still be within the product identification and calibration or product-use or expiration determination methods contemplated by the present invention. For example, an alternative is to detect the minute magnetic field generated by the polarized .sup.3 He spins.

Detailed Description Text (58):
For transport units comprising a plurality of gas chambers 30 (not shown) it is preferred that an individual NMR coil 75 be positioned adjacent each gas chamber within the transport unit 10. It is further preferred that each gas chamber 30 be substantially electrically isolated from the other gas chambers 30, such that each gas chamber 30 is individually monitorable (individually excitable) for hyperpolarization level and each is individually tunable (adjustable field strength and coil current) according to the corresponding NMR coil 75, as will be discussed further below.

Detailed Description Text (61):
As shown in FIG. 5, the top of the gas chamber 61A is hinged to the bottom 60B which defines the housing 60. The top 61A includes latches 200A, 200B which engage with corresponding components 210A, 210B positioned on the outside wall of the bottom of the housing structure. Preferably, the transport unit 10 defines an enclosed volume 65 for holding the solenoid 20, the gas chamber 30 and the proximately positioned NMR coil 75 therein. Preferably, the enclosure 65 and, indeed, the entire transport unit 10, is configured and formed to be polarization friendly (substantially devoid of paramagnetic and ferrous materials) such that the transport unit 10 does not induce significant reductions in the polarization level of the hyperpolarized gas therein. One suitable housing 60 is a relatively compact aluminum case (having about a 5 mm wall thickness) manufactured by Zero Enclosures of Salt Lake City, Utah and was modified to substantially remove ferromagnetic hardware.

Detailed Description Text (62):
In its preferred position, as shown in FIG. 2, the solenoid 20 is cylindrical and is oriented such that it extends longitudinally from the opposing top and bottom ends of the transport unit 10. The coil segment(s) are circumferentially wrapped around the respective portions of the cylindrical wall of the solenoid core and are preferably configured such that the magnetic holding field B.sub.H is directed downward such that it aligns with the predominant direction of the earth's magnetic. As such, the current in the solenoid coil segment(s) is directed clockwise when viewing the solenoid 20 from the top of the transport unit. This directional alignment with the earth's dominant magnetic field can maximize the effect of the holding field at any given current. The solenoid 20 preferably includes a metallic coating (such as a layer of foil tape) 24 formed on or positioned on the inner surface (the surface proximate to the hyperpolarized gas) of the solenoid 20.

Detailed Description Text (64):
Preferably, for transit purposes, the transport unit power source 40 is a 12V DC battery (such as those used to power motorcycles). However, at docking stations or an end-use site, the transport unit 10 can be conveniently plugged into an exterior

power source to bypass and preserve the battery charge. Also preferably, as will be discussed further below, the transport unit power source 40 is configured via operating circuitry 50 to provide an adjustable current supply to the solenoid 20 of from about 100 mA to about 1.7 or 2 A. Thus, the solenoid 20 is preferably configured to provide a magnetic holding field of between about 2 to 35 gauss.

Detailed Description Text (66):
Preferably, the gas chamber 30 is configured to provide a quantity of hyperpolarized gas which can be conveniently delivered to an end point in a user-friendly single dose volume (but of course can also be configured to provide multiple or partial dose quantities) of hyperpolarized gas. In a preferred embodiment, the gas chamber is a 100-200 cm.sup.3 gas spherical chamber 30. For .sup.3 He it is preferred that the gas chamber 30 be pressurized to about 4-12 atmospheres of pressure, and more preferably it is pressurized to about 5-11 atmospheres of pressure for storage and transport to provide a single or double dose quantity of hyperpolarized gas. Pressuring an appropriately sized gas chamber 30 can allow the hyperpolarized gas to be released through the exit port 31 as the pressure acts to equalize with ambient conditions. Thus, by merely opening the valve 32, the hyperpolarized gas can be directed via the exit port 31 to a patient or a patient delivery system with minimal handling (and thus potentially depolarizing interaction). It should be noted that for hyperpolarized .sup.3 He, at about 10 atm of pressure the theoretical T.sub.1 is about 75 hours. Substantially higher pressures allow more product to be shipped in the container and reduces the sensitivity of the hyperpolarized gas to gradient relaxation, but the gas-gas collision relaxation can become substantial. In contrast, for .sup.129 Xe, it is preferred that the gas pressure be about 1 atm or less, because higher pressures can dramatically reduce the expected relaxation time of the hyperpolarized .sup.129 Xe (i.e., at 10 atm, T.sub.1 =5.6 hours).

Detailed Description Text (67):
In a preferred embodiment of the instant invention, as shown in FIG. 2, the gas chamber 30 is rigid and includes a capillary stem 35 which is sized and configured to minimize the travel of hyperpolarized gas atoms out of the spherical volume and acts to keep most of the hyperpolarized gas away from the valve 32. As such, a major portion of the hyperpolarized gas remains in the region of highest homogeneity within the solenoid 20 where it is best protected from depolarizing effects during transport. Preferably, the capillary stem 35 includes about a 1.0 mm inside diameter and has a length which is sufficient to allow proper positioning of the sphere within the region of homogeneity in the solenoid 20. In a preferred embodiment of the solenoid 20 described above, the capillary stem 35 is approximately 4 inches long. The capillary stem 35 is dimensioned such that the ratio of the chamber volume to the capillary volume is such that the diffusion time for .sup.3 He at fill pressure (the time it takes for the .sup.3 He to traverse the stem length twice) is much greater than the desired T.sub.1. Also preferably, the inner diameter of the capillary stem 35 is sufficiently small as to minimize contact of the hyperpolarized atoms with the valve 32 thereby keeping a substantial portion of the hyperpolarized gas in the spherical volume 33 and thus within the high-homogeneity field region.

Detailed Description Text (69):
FIG. 9 schematically illustrates a preferred portable monitoring system 100 and transport unit 10 combination apparatus. As shown, the portable transport unit 10 includes the power monitoring circuit 325, the power source 40, the solenoid current input 360, the NMR coil 75, the magnetic field generator 300 (FIG. 2 illustrates this as a solenoid 20). The magnetic field is applied to surround the hyperpolarized gas 200 in a gas chamber 30. The combination apparatus also preferably includes a user input 380 and a display 351. As also shown, the portable monitoring system 100 is engaged with the transport unit 10 and includes a computer 500, a pulse generator 115, a signal analyzer 110, a display 160, a user input 140, and an alarm 327.

Detailed Description Text (70):
Establishing NMR Coil Resonance for Optimizing Gas Monitoring Frequency

Detailed Description Text (71):
The NMR coil 75 has an associated coil resonance which typically varies unit to unit (corresponding to various parameters such as lead length, BNC coupling and coil configuration). The NMR coil 75 resonance is important because it can affect the optimal transmit and receive frequency used to obtain more accurate readings of the level of hyperpolarization associated with the hyperpolarized gas. In order to determine the optimal receive and transmit frequency, the NMR coil 75 resonance is preferably determined from a coil ring-down as described below.

Detailed Description Text (72):
The NMR coil 75 can be electrically modeled as an inductor-capacitor circuit ("L-C circuit"). Therefore, the particular NMR coil 75 resonance can be determined by pulsing the NMR coil 75 with an excitation electrical pulse and letting the circuit "ring-down". For example, an electrical signal responsive to the excitation pulse will decay according to the L-C circuit model. Therefore, a coil-ring down reading can be taken to establish the optimal frequency which can be used to obtain the most sensitive or highest response from the hyperpolarized gas. The coil ring down can be done either in the presence of the hyperpolarized gas or in the absence of hyperpolarized gas (preferably at use temperature such as at ambient or room temperature) to establish a base-line coil resonance. If taken in the presence of the hyperpolarized gas, the magnetic field is increased to shift the frequency of the gas signal up so that the gas signal does not interfere with the coil signal of interest.

Detailed Description Text (73):
In operation, the NMR coil 75 resonance may change over time. For example, the resistance of the wire of the coil may vary depending on the attendant temperature. Therefore, it is preferred that the optimal frequency be determined at least just prior to transport, to assure that an optimal response frequency is set for the NMR coil to adjust for the coil variation and provide a more accurate reading of the gas polarization level. It is also preferred that any monitoring method transmit and receive the excitation signal at the optimal frequency when determining the actual polarization level of the hyperpolarized gas in order to obtain a more accurate signal value corresponding to the polarization of the hyperpolarized gas. Thus, in transit, the holding field strength can be changed (preferably adjusted by changing the current supplied to the solenoid 20) to obtain the resonance of the NMR coil 75. Other methods can be used to force the receive signal to an optimal frequency such as the lookup chart described above.

Detailed Description Text (75):
Advantageously, by shortening the post-mute signal so that it has a delay of less than 3 ms and preferably about or less than 1 ms, the coil-responsive data can be evaluated to represent the NMR coil ring down independent of ambient field strength. From this post-mute data, the resonance of the NMR coil 75 can be established and an "optimal" gas excitation transmit and receive frequency can be determined.

Detailed Description Text (76):
Assuming that 24 kHz is the optimal frequency, in operation, a gas excitation pulse is transmitted to the gas at 24 kHz. The received signal corresponding to the response of the gas is preferably received at this same optimal frequency, 24 kHz in this example. However, the receive mode is somewhat passive and harder to directly control. Thus, typically the received signal may be offset above or below the optimal frequency, such as at 23.5 kHz in this example. Preferably, the field strength is adjusted (here raised) to assist/force the gas-related receive signal to be at 24 kHz. By setting the receive signal to the optimal frequency, a more

accurate reading of the actual polarization of the gas can be obtained.

Detailed Description Text (78):
In a preferred embodiment, the software included in the monitoring system 100 of the present invention can automatically determine when a receive signal frequency adjustment is needed and thus provide an "automatic" polarization adjustment to yield a more accurate polarization level of the gas. In addition, or alternatively, a manual or user input can also be used. In any event, the software is preferably operably associated with the NMR coil 75 and solenoid 20 to be able to adjust the solenoid current based on desired field strength and/or NMR coil 75 resonance factors.

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CLAIMS:

1. A method of monitoring the polarization of hyperpolarized gas, in transit, using NMR and/or MRI comprising the steps of: generating a magnetic holding field having a region of homogeneity; transporting a quantity of hyperpolarized gas from a first site to a second site in a shielded portable transport container configured to encase a vessel holding the hyperpolarized gas therein in a manner which inhibits the depolarization of the hyperpolarized gas during transport; transmitting a predetermined excitation pulse during the transporting step to the quantity of hyperpolarized gas at least once during said transporting step; receiving a NMR and/or MR response signal corresponding to the response of the hyperpolarized gas to the excitation pulse during the transporting step; and determining the level of polarization of the hyperpolarized gas based the received response signal.

2. A method according to claim 1, wherein said transmitting, said receiving, and said determining steps are repeated during said transporting step.

3. A method according to claim 1, wherein said transmitting, said receiving and said determining steps are repeated a plurality of times including at least once before, at least once during, and at least once after said transporting step, and wherein said method further comprises the step of selecting the excitation pulse such that a plurality of transmitted pulses are substantially non-depolarizing to the quantity of hyperpolarized gas.

4. A method according to claim 1, wherein said determining step includes the step of analyzing the received signal to account for temporal magnetic field variations, thereby providing a more accurate polarization measurement value for the hyperpolarized gas.

5. A method according to claim 4, wherein said analyzing step includes adjusting the frequency value corresponding to the received signal response to correct for frequency shifts away from a predetermined frequency.

7. A method according to claim 5, wherein for .sup.3 He and a magnetic holding field strength of about 7 gauss, the pulse frequency is in the range of about 20-50kHz.

8. A method according to claim 1, further comprising the step of displaying information in a format readable by a user regarding one or more of external environmental conditions, magnetic holding field strength, magnetic holding field fluctuation, and the polarization level of the gas.

9. A method according to claim 1, wherein said method is performed by a portable electronic device which is operably engaged with a portable transport unit, the transport unit having a solenoid with a plurality of coil segments which provide the magnetic holding field in response to electrical current introduced thereto, wherein the transport unit performs the step of generating a magnetic holding field, and wherein said generating step is performed such that the magnetic holding field has a field strength which substantially shields the hyperpolarized gas from the potential effect of stray magnetic field gradients during said transporting step, thus inhibiting depolarization of the hyperpolarized gas.

10. A method according to claim 9, further comprising the steps of; detecting magnetic field fluctuations in the magnetic holding field; and adjusting the electrical current introduced into the solenoid so as to compensate for magnetic field fluctuations in the magnetic holding field.

13. A portable monitoring system for determining the polarization level of a quantity of hyperpolarized gas product in transit using NMR and/or MRI, comprising: positioning a NMR coil proximate to a quantity of hyperpolarized gas-based product, the NMR coil and hyperpolarized gas-based product being packaged for movement; transporting the quantity of hyperpolarized gas-based product with the NMR coil from a first site to a second site remote from the first site after said positioning step; transmitting an excitation pulse to the NMR coil to excite a small amount of the hyperpolarized gas-based product during said transporting step; receiving an electrical NMR and/or MR based response signal associated with the hyperpolarized gas-based product corresponding to said transmitting step during said transporting step; and analyzing the response signal to determine the polarization level of the hyperpolarized gas product during said transporting step.

16. A portable monitoring system according to claim 13, wherein the NMR coil has an associated coil resonance, and wherein said analyzing step includes the steps of evaluating the received response signal and adjusting for the NMR coil resonance thereby more accurately determining the polarization of the hyperpolarized gas product.

17. A portable monitoring system according to claim 16, wherein said analyzing step is performed by monitoring the received response signal value to determine the need for adjusting the received value with a predetermined correction factor.

18. A portable monitoring system according to claim 16, wherein the hyperpolarized gas product is held within a transport unit having a longitudinally extending solenoid coil and a current input therefor, and further comprising an adjustment means for compensating the current to the solenoid thereby adjusting the field strength of a magnetic holding field which is positioned such that it is operably associated with the quantity of hyperpolarized gas during transport.

19. A portable monitoring system according to claim 18, wherein said adjustment means compensates for detected magnetic holding field strength fluctuations.

21. A computer program product for monitoring and/or determining the polarization level of hyperpolarized noble gas in transit using NMR and/or MRI, the computer program product comprising: a computer readable storage medium having computer readable program code means embodied in said medium, said computer readable program code means comprising: computer readable program code means for selecting an excitation pulse; computer readable program code means for transmitting the selected excitation pulse to a quantity of hyperpolarized gas held in a transport container via an NMR coil positioned proximate thereto while the hyperpolarized gas is in transit to a use site; computer readable program code means for analyzing a received NMR and/or MR signal associated with the response of the hyperpolarized noble gas product to the excitation pulse while the hyperpolarized gas is in transit to a use site; computer readable program code means for adjusting the received response signal such that it more accurately corresponds to the hyperpolarization level of the hyperpolarized gas; and computer readable program code means for determining the polarization level of the hyperpolarized gas in transit and/or subsequent thereto.

22. A computer program product for monitoring and/or determining the polarization level of a hyperpolarized gas product according to claim 21, further comprising: computer readable program code means for generating a correction factor table corresponding to a Fourier transform of an NMR coil response to an RF pulse; and computer readable program code means for applying a correction factor from the correction factor table to a received signal response value to produce a more accurate polarization measurement.

23. A computer program product for monitoring and/or determining the polarization

level of a hyperpolarized gas product according to claim 22, further comprising: computer readable program code means for allowing a user to select excitation pulse parameters; and computer readable program code means for displaying the determined polarization level value.

24. A computer program product for monitoring and/or determining the polarization level of a hyperpolarized gas product according to claim 22, further comprising: computer readable program code means for determining the elapsed transit time or time from original polarization of the quantity of hyperpolarized gas product.

25. A computer program product for monitoring and/or determining the polarization level of a hyperpolarized gas product according to claim 21, wherein said computer program product is configured to generate polarization values in response to excitation of the NMR coil during physical transport of the hyperpolarized gas from one location to a second location remote from the first location.

26. A computer program product for monitoring and/or determining the polarization level of a hyperpolarized gas product according to claim 21, further comprising: computer readable program code means for generating an alarm when the computed polarization value is below a predetermined level.

27. A computer program product for monitoring and/or determining the polarization level of a hyperpolarized gas product according to claim 26, wherein a magnetic holding field having an adjustable electric current input is applied to a region proximate to the hyperpolarized noble gas product, and further comprising computer readable program code means for adjusting the amount of current supplied to the current input.

28. A computer program product for monitoring and/or determining the polarization level of a hyperpolarized gas product according to claim 21, further comprising: computer readable program code means for analyzing a predetermined number of sequential response signal sample values associated with a decaying received signal and comparing the received signal sample values to predicted values and adjusting the value of the received signal sample values corresponding to the comparing step with predetermined correction values associated with an optimal transmit and/or receive frequency.

29. A computer program product for monitoring and/or determining the polarization level of a hyperpolarized gas product according to claim 23, wherein said means for adjusting is responsive to determination of magnetic field fluctuation proximate to the hyperpolarized gas in the transport unit.

30. A portable system for monitoring hyperpolarized gas during transit and/or transit and storage using NMR and/or MRI, comprising: a portable transport unit configured to hold a quantity of hyperpolarized gas in a container held therein; a NMR coil configured and sized to be positioned in said portable transport unit such that it is proximate to the quantity of hyperpolarized gas; a pulse generator operably associated with said NMR coil for generating an excitation pulse to a portion of the hyperpolarized gas; transmit means operably associated with said pulse generator and said NMR coil for transmitting the excitation pulse to the hyperpolarized gas; receive means operably associated with said NMR coil for receiving a NMR and/or MR response signal corresponding to the response of the hyperpolarized gas to the transmitted excitation pulse; and a signal analyzer operably associated with said receive means, said analyzer including a computer readable program code means for determining the polarization level of the hyperpolarized gas; wherein said NMR coil, said transport unit, said pulse generator, and said transmit and receive means are configured to be operative so as to receive the response signal during transport or transport and storage of the hyperpolarized gas away from the original polarization site and away from the patient hyperpolarized gas delivery location.

31. A portable system for monitoring hyperpolarized gas according to claim 30, wherein said portable transport unit comprises a solenoid configured to generate an adjustable electromagnetic holding field proximate to the quantity of hyperpolarized gas product, wherein said adjustable holding field corresponds to the amount of electric current directed into said solenoid, and wherein said portable monitoring apparatus further comprises a power monitoring circuit configured to control the amount of current directed to said solenoid.

32. A portable system for monitoring hyperpolarized gas according to claim 31, wherein said power monitoring circuit is configured to alter the amount of electrical current introduced into said solenoid based on detected fluctuations in the magnetic holding field.

34. A portable system for monitoring hyperpolarized gas according to claim 32, further comprising computer program code means for displaying information regarding one or more of the excitation pulse parameters, the magnitude of the magnetic holding field, and the polarization level of the hyperpolarized gas product.

35. A portable system for monitoring hyperpolarized gas according to claim 31, further comprising a user input device for allowing a user to select one or more of the excitation pulse parameters, the field strength of the magnetic holding field, and the current input to said solenoid.

36. A portable system for monitoring hyperpolarized gas according to claim 30, wherein said signal analyzer includes computer program code means for adjusting the measured value of the received signal corresponding to predetermined correction factor values.

37. A portable system for monitoring hyperpolarized gas according to claim 36, wherein the adjustment corrects the measured value of the received signal by applying a predetermined correction factor value.

38. A portable system for monitoring hyperpolarized gas according to claim 36, wherein the predetermined correction factor values correspond to the response of the NMR coil at selected operational frequencies.

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L11: Entry 10 of 17 File: USPT Aug 8, 2000

DOCUMENT-IDENTIFIER: US 6100688 A
TITLE: Methods and apparatus for NQR testing

Abstract Text (1):
A method and apparatus for imaging within a sample space an object containing quadrupolar nuclei comprises irradiating the object to excite nuclear quadrupole resonance, applying to the object a magnetic field gradient having a profile Bo(x) such that the square of the profile (Bo(x))2 varies linearly with distance (x), detecting resonance response signals from the nuclei, and deriving an image from the response signals. A method of and apparatus for nuclear quadrupole resonance testing an object, and a method of and apparatus for detecting the presence of a particular substance containing a given species of quadrupolar nucleus, are also disclosed.

Brief Summary Text (3):
The present invention relates to a method of and apparatus for imaging within a sample space an object containing quadrupolar nuclei. The object may, for instance, be a human or animal body or a part thereof; the image may be a simple spin-density image or may be a temperature, pressure or electric field distribution image. For convenience the imaging referred to above will be called NQR imaging. The-present invention also relates to a method of and apparatus for NQR testing an object, and to a method of and apparatus for detecting the presence of a particular substance containing a given species of quadrupolar nucleus.

Brief Summary Text (5):
Methods for producing imaqes from the resonances of spin-1/2 nuclei which have a magnetic moment but no electric quadrupole moment have been extensively developed and described in various books (e.g. P. Mansfield and P. G. Morris, "NMR Imaging in Biomedicine", 1982, Academic Press). Such methods may use linear magnetic field gradients superimposed on a strong, uniform magnetic field. The resonance frequencies of the spin-1/2 nuclei are linearly dependent on the total magnetic field; this is made to vary linearly with distance across the sample, and the distribution of the substance concerned is derived from the frequencies in the signals produced. Such techniques are commonly called NMR imaging.

Brief Summary Text (6):
Methods for imaging using the resonances of quadrupolar nuclei (which have I.gtoreq.1) would be expected to have several advantages. Firstly, the quadrupolar resonances can be detected without using the strong, uniform magnetic field which is needed to make the magnetic resonances of spin-1/2 nuclei conveniently detectable. Hence the relatively large, expensive and sample-size-limiting magnet structures which are necessary for NMR imaging will not be needed. Avoiding the need for this strong magnetic field also avoids the substantial complications and possible distortions caused by non-uniformity in the field and magnetic interference produced in practical NMR equipment. Secondly, the quadrupolar resonances are more definitely or characteristically associated with specific chemical environments, and it is therefore easier to distinguish results which are due to a particular substance from effects which are due to other substances present in the sample. Methods in which quadrupolar resonances might be observed directly rather than through their interactions with magnetic resonances would be

highly suitable for medical use because they do not require patients to be exposed to rapidly changing strong magnetic fields.

Brief Summary Text (7):
Possible disadvantages or limitations on NQR imaging are that the nuclei may be less abundant, may have nuclear quadrupole resonance frequencies lower than the magnetic resonance frequencies of the protons commonly used in NMR imaging, and may have smaller gyromagnetic ratios. This can create a sensitivity problem which has two aspects. Firstly, it may be difficult to achieve a degree of excitation of the quadrupolar nuclei comparable with the excitation of the spin-1/2 nuclei which is commonly used in NMR equipment. The radiofrequency power used in medical applications must be limited to avoid undue heating and damage to living tissue. Secondly, the response signals will be weak and of low signal-to-noise ratio, needing

Brief Summary Text (9):
To our knowledge methods for imaging using quadrupolar resonances have as yet had very little development. Rommel et al (J. Magnetic Resonance 91, 630-636, 1991) reported theoretical reasoning with a conclusion that there would be great practical difficulties in any attempt to use such methods to derive any image from the interaction of a magnetic field gradient with quadrupolar nuclei, considering in particular half-integral spin nuclei of I.gtoreq.3/2. As an alternative they reported a method in which the strength of a radiofrequency excitation was varied across a sample in zero magnetic field.

Brief Summary Text (10):
Matsui et al. (J. Magnetic Resonance 88, 186-191, 1990) reported measurements on .sup.35 Cl nuclei in sodium chlorate in a linear magnetic field, in which an image was derived from the effects of the field on the spectral shape and width of the resonance. It appears that this may be a special case; the .sup.35 Cl nuclei have I=3/2 and their asymmetry parameter in sodium chlorate is zero. Matsui et al. state that "it is practically impossible" for the magnetic field to shift the resonance frequency. This may be incorrect, at least in relation to nuclei other than .sup.35 Cl in substances other than sodium chlorate.

Brief Summary Text (12):
According to one aspect of the present invention, in general terms there are provided methods and apparatus for producing an image representing the distribution of a specific substance or local temperatures within an article or in part of a human or an animal body, wherein the article or part of the body is irradiated with a pulse or pulses of radiofrequency energy at or close to a quadrupole resonance frequency of atomic nuclei of I.gtoreq.1 in the specific substance and is subjected to at least one magnetic field gradient having a profile which produces a variation (including possibly a splitting) of the resonance frequency which is a linear function of distance in the direction of the magnetic field gradient, response signals from the nuclei are measured and an image is derived by data processing the result of many such tests. According to the invention, preferably either the magnetic field profile is a function B.sub.o (x) of distance x such that its square [B.sub.o (x)].sup.2 is a linear function of x, within a limited sample volume of the article or body, or else the invention relates to a method of imaging using quadrupolar nuclei having integral spin quantum number (I=1, 2, 3, . . .), preferably having unity spin quantum number. .sup.14 N is a nucleus for which I=1.

Brief Summary Text (13):
According to an aspect of this invention, there is provided apparatus for imaging within a sample space an object containing quadrupolar nuclei, comprising means for irradiating the object to excite nuclear quadrupole resonance, means for applying to the object a magnetic field gradient having a profile B such that B.sup.n varies linearly with distance, n being greater than one, means for detecting resonance response signals from the nuclei, and means for deriving an image from the response

signals.

Brief Summary Text (14):
The apparatus may further comprise means for applying to the object a magnetic field gradient having a profile which varies linearly with distance.

Brief Summary Text (15):
This invention arises from our discovery that, surprisingly, for a wide range of substances containing quadrupolar nuclei, a gradient profile having n greater than one (rather than a linear gradient) should be used in NQR imaging since it (rather than a linear gradient) produces a variation in resonance frequency which is a linear function of distance. As will be apparent from the following, for many (possibly the majority of) applications we have discovered that n should be 2 (i.e. a square law gradient), by which is meant that n should be exactly, or close to, two.

Brief Summary Text (16):
Magnetic field gradients in different directions may be applied in sequence to derive sufficient results for the derivation of a two-dimensional or three-dimensional image, each gradient having a profile which makes the resonant frequency vary as a linear function of distance in the direction of the gradient. Where gradients in only two directions are used, the sample or article may be rotated about one of these directions to derive information sufficient for three-dimensional imaging.

Brief Summary Text (18):
The quadrupole resonance frequencies are also shifted by temperature variations, and by comparing tests with different magnetic field profiles the technique may be extended to produce images representing the variations of temperature in a sample or body part. This can provide a non-invasive method for measuring or monitoring localized temperatures within a sample or body part, and it may be useful in monitoring and/or controlling treatments which involve localized heating. Imaging of pressure or electric ield variations may be effected following the same principle.

Brief Summary Text (19):
In the sub-molecular environment of compounds or crystals, the nature and disposition of the adjacent electrons and atomic nuclei produce electric field gradients which modify the energy levels and the resonance frequencies of the quadrupolar nuclei. The symmetry or asymmetry of these local electric field gradients is an important factor in any study of nuclear quadrupole resonance, and it is measured by an asymmetry parameter n which can have values from zero to one. For instance, for the ring nitrogen in the explosive RDX, .eta..apprxeq.0.62, whilst for the peptide nitrogen in amino acids and polypeptides .eta..apprxeq.0.4; the nitrogen in cocaine and heroin is thought to have .eta..ltoreq.0.1. The spin quantum number I is another controlling factor. .sup.14 N and .sup.2 H nuclei have I=1; nuclei such as .sup.11 B and .sup.75 As have I=3/2, and .sup.17 O and .sup.27 Al I=5/2, etc.

Brief Summary Text (21):
When first and second-order perturbation theory are applied to a study of these resonance frequencies in an externally applied magnetic field, it appears that there are substantially two cases which can be represented by different mathematical approximations.

Brief Summary Text (22):
For such nuclei in substances having n>0.1, over a considerable range of magnetic field strengths the resonance frequencies of individual nuclei may be expressed by equations, derived from a paper by S. Pissanetzky (Zeeman effect of .sup.14 N nuclear quadrupole resonance with polycrystalline samples, J. Chem. Phys., Vol. 59,

No. 8, p. 4197, 1973), of the form

Brief Summary Text (23):
where G=.gamma./2.pi., .gamma.=the gyromagnetic ratio, and K=.vertline.e.sup.2 qQ/4h.vertline., e.sup.2 qQ/h being the quadrupole coupling constant. F.sub.x, F.sub.y and F.sub.z are functions involving .eta. and the two polar angles (.theta.,.phi.) specifying the relative orientation of the local electric field gradient with respect to the direction of the applied magnetic field B. Since in general there will be many molecules randomly oriented with respect to the direction of the applied magnetic field, there will be many nuclei with a range of values of F.sub.x, F.sub.y and F.sub.z and consequently a range of resonant frequencies from each location with any non-zero value of B; the resonance is broadened. However, the maximum value of the dominant term in the expressions for F.sub.x, F.sub.y and F.sub.z is proportional to 1/.eta., and hence this broadening is comparatively limited for substances which have a relatively high asymmetry parameter .eta..

Brief Summary Text (24):
It is possible with much computation to calculate how the resonances of a population of randomly-oriented nuclei will combine to determine the line shape and frequency shift of their observable resonance effect.

Brief Summary Text (25):
The results of our researches are that, in general, the observable resonances will show a frequency shift proportional to B.sup.2 with a gradual broadening of the line shape, until a critical field strength B.sub.2 is reached; above this field strength the line shape becomes distorted and the frequency shift gradually departs from a strict B.sup.2 dependence. The angle .alpha. between the directions of the magnetic field B and the radiofrequency excitation field B.sub.1 has a significant effect on the onset and nature of these changes, and it affects different lines differently.

Brief Summary Text (26):
We have conducted experiments using pure substances in a uniform magnetic field of adjustable strength to study how the field strength alters the line shape and shift. From such experiments using samples of various explosives containing .sup.14 N nuclei such as RDX (for the ring .sup.14 N of which .eta.=0.62). We have found that the resonant frequency .omega..sub.x does shift in proportion to B over a substantial range of magnetic field strengths. We have also found that above a certain field strength, the resonances we have studied develop a doublet structure when B is perpendicular to B.sub.1. Fine structure is also indicated in the results published by Matsui et al. though they did not comment on it. In the case of RDX, both components of the doublet shift in proportion to B.sup.2. with different rates; we would expect the same to be true for other substances.

Brief Summary Text (27):
Hence for NQR imaging of nuclei having I=1 in substances having .eta.>0.1, it is preferable to use a magnetic field profile B(x) such that

Brief Summary Text (34):
Hence, for a majority of the substances of practical interest with nuclei having integral spin quantum number, a magnetic field profile of the form given in Equation 5 is appropriate.

Brief Summary Text (35):
However, there may be some substances for which (GB cos .theta./(.eta.K)).sup.2 is near unity and for which therefore the above analysis does not hold. Sometimes, dependent on the substance, a profile substantially of the form given in Equation 5 would still be appropriate, with any slight deviations from a precise B.sup.2 dependence being accommodated by appropriate minor adjustments to the field

gradient profile to give a linear frequency shift. In other circumstances the deviations from a B.sup.2 dependence may be so significant that a completely different gradient profile may need to be employed. Such a profile would normally be somewhere between square law and linear (that is, 1<n<2, where n is the power of the profile referred to previously), although there may be some cases where n is actually greater than two.

Brief Summary Text (36):
The case of nuclei having half integral spin quantum number is now considered. I=3/2 nuclei are taken as a representative example, but the principles behind the following analysis, and the conclusions drawn from the analysis, apply to all half integral spin systems. Nuclei with I=3/2 in a single crystal structure in a weak magnetic field B have four quadrupole resonance frequencies given by equations of the form

Brief Summary Text (37):
where E is a function of .gamma. and .eta. and the four resonances have different functions F.sub.n. This leads for single crystals to frequency shifts linearly dependent on the magnetic field strength B.

Brief Summary Text (38):
Hence a linear magnetic field profile will be appropriate for imaging nuclei with I=1, 2, 3 . . . etc. when (GB cos.theta.)(.eta.K)).sup.2 >>1 or nuclei with I=3/2, 5/2, etc. in a single crystal structure. This can be provided by coils in the anti-Helmholtz or Maxwell configuration--two coils of radius R, spaced R apart and connected to produce opposing fields. A system providing linear gradient fields in three orthogonal directions will have three pairs of identica coils symmetrically arranged about the sample space. In such a system complementary magnetic field profiles can be provided by simply reversing the direction of the currents. Such systems may be suitable, for instance, for the imaging of parts of human arms or legs and possibly heads; they should be simpler and less expensive than present NMR imaging instruments.

Brief Summary Text (39):
For substances with I=3/2, 5/2, etc. other than single crystal structures, the dependence of resonance frequency on magnetic field becomes complex and not readily amenable to theoretical analysis. In these circumstances, we propose that the relationship between resonance frequency and magnetic field is predetermined for a specific substance of interest and stored as a "look-up" table. Then a magnetic field profile of the form given in

Brief Summary Text (40):
Equation 5 (or otherwise a linear field gradient) may be employed to produce spatial encoding. The image can be derived by appropriate use of the look-up table. Alternatively, a field profile, such as would produce a variation of resonance frequency which is substantially a linear function of distance in the direction of the magnetic field gradient, could be utilised. This profile would usually have a form somewhere between linear and square law (that is, 1<n<2).

Brief Summary Text (41):
By employing the magnetic field profiles described above known methods of NMR imaging can be adapted to NQR imaging, the major simplification being the elimination of the strong background magnetic field which is necessary for NMR experiments.

Brief Summary Text (42):
In NMR imaging it is usual to use radiofrequency pulses of sufficient power to cause a 90.degree. rotation of the magnetisation of the nuclei. The pulse duration t.sub.w is given by the equation ##EQU1## where B.sub.1 is the peak strength of the radio frequency excitation field. There will be other constraints on the pulse

duration and so in effect this equation often sets the power required. In NQR experiments the corresponding condition for polycrystalline samples containing spin-1 nuclei is ##EQU2## The gyromagnetic ratio .gamma. will usually be much smaller for quadrupole nuclei than for protons, so that the r.f. field strength and power required to satisfy equation (11) will be much greater than that required to achieve the corresponding conditions in NMR imaging of protons. Hence it may be practically preferable or necessary to use pulses of considerably lower power and rotation angle, and to make up for this by accumulating results from more pulses, and probably applying pulses more frequently, so that the interval between pulses (.tau.) is less than the spin-lattice relaxation time (T.sub.1). This may be particularly necessary to avoid tissue damage in medical applications. This will also make the accumulated signal strength less sensitive to variations in the rotation angle over the sample space. Shaped or phase/amplitude modulated pulses can also assist in reducing the r.f. power.

Brief Summary Text (43):
The projection-reconstruction methods of imaging developed from the work of Lauterbur (Nature 242, 190-191, 16/3/73) may be preferred for medical applications as they require only small step-wise changes in the magnetic field gradients.

Brief Summary Text (44):
Variations of temperature may cause frequency shifts comparable with the frequency shifts caused by the magnetic field. This will cause distortion in images of samples which have an inhomogeneous temperature distribution, but this can be corrected. This effect may also be used to advantage as a non-invasive means for imaging or monitoring the temperature distribution within the sample. Over a small temperature range, the variation in frequency is often linear with respect to temperature.

Brief Summary Text (45):
Fourier transformation of a set of results taken in zero magnetic field with a sufficiently short r.f. pulse will therefore give a spectrum which, when compared with one or more spectra of a homogenous uniform temperature sample of the relevant substance, will indicate the range of temperatures present.

Brief Summary Text (46):
Increasing temperature generally shifts the resonances to a lower frequency, so that in any image produced by excitation of the frequency .omega..sub.x without temperature correction, indications of the nuclear density in any hot spot will appear displaced towards the region of lower magnetic field. Repeating the experiment with the field profile reversed (or complementary) will cause the hot-spot signal to appear displaced in the opposite direction, and comparison with the previous image will indicate the position of the hot spot and its temperature.

Brief Summary Text (47):
Variations of pressure or electric field will also cause frequency shifts which may be utilized for imaging purposes.

Brief Summary Text (48):
Where the magnetic field splits any resonance into a multiplet, or where there are two or more resonant frequencies close together, it is advantageous to use excitation signals having a frequency distribution broad enough to excite all resonances or all parts of the multiplet. The response signals will then show a pattern of slow beats at the difference frequencies. In certain cases, e.g. when the line is a simple doublet, it may be desirable to use the frequency of these slow beats as the characteristic to be measured, rather than the frequency of either resonance, because it will usually be more sensitive to variations in field strength and it may be more readily distinguishable.

Brief Summary Text (59):

Preferably, the resonance frequencies are components of a multiplet. A multiplet usually connotes two or more resonance frequencies which are relatively close together (usually within a few percent of each other) and are yet well-resolved. Multiplets may arise, for instance, due to crystallographic non-equivalence of otherwise structurally identical NQR nuclei (as is the case with, for example, RDX, TNT and HMX); they may also arise (e.g. Heroin and Cocaine) due to the nearly axially symmetric electric field gradient in which the NQR nuclei are located.

Brief Summary Text (65):
Preferably, the alarm signal is provided in further dependence on whether the relative intensities of the response signals at each of the plurality of resonance frequencies match those which would be expected for the particular substance. This measure can further reduce the number of false positives. It is envisaged that this measure may suitably be put into practice by predetermining in separate tests the relevant characteristics of the particular substance and storing these for use in the field.

Brief Summary Text (67):
Since resonance frequency varies with temperature, pressure or magnetic field, it may be necessary to take such variations into account by irradiating over a range sufficient to cover all possible variations of resonance frequency which might in practice be encountered.

Brief Summary Text (69):
In the case of RDX (cyclo-trimethylenetrinitramine) the multiplicity produced by crystallographic non-equivalence of otherwise structurally identical nitrogen nuclei can be exploited. In the vapor phase, the molecule is said to have C.sub.3.nu. symmetry, but this is lost in the solid state, and all three .sup.14 N quadrupole resonance lines from the ring nitrogen nuclei are well-resolved triplets. The splittings are small (less than 150 kHz for .nu..sub.x near 5.100 kHz), and, although the individual frequencies vary with temperature, the splittings themselves are almost independent of temperature between -30 and +30.degree. C., varying from 143.52 kHz at the former to 145.49 kHz at the latter.

Brief Summary Text (71):
After each pulse or pulse sequence at a given frequency, the NQR instrument will analyse the absorption peak for its frequency, height, width and area, taking into account possible errors assessed from the noise measured off-resonance. In this example, only if statistically equivalent responses are detected after each excitation frequency has been excited would the instrument provide an alarm signal.

Brief Summary Text (72):
The above technique can be highly discriminatory against noise peaks and interference; only RDX will give equal, or nearly equal, response signals at the three selected frequencies at a given temperature.

Brief Summary Text (74):
a close doublet (.nu..sub.x, .nu..sub.y) near 3,900 kHz and Cocaine a doublet near 960 kHz. In these cases, the splitting arises from the nearly-axially symmetric electric field gradient in which the .sup.14 N nucleus is located, and not from resolved crystallographic non-equivalence. The present invention still applies, and the signal-to-noise ratio may be increased by .sqroot.2 in these two cases, although the lines are not completely independent.

Drawing Description Text (3):
FIGS. 1 and 2 are diagrammatic representations of alternative electromagnet coil configurations which may be used to produce a magnetic field profile B(x) such that [B(x)].sup.2 varies as a linear function of distance x;

Detailed Description Text (2):
FIG. 1 shows in axial section two coils 1 and 2 which have the same mean radius R and are spaced a distance R apart on a common axis 3. Coil 1 will have twice the ampere-turns (ni) of coil 2, the current directions being the same so that their fields are in the same direction. If distance along the axis from the plane of coil 1 is denoted by x, this arrangement produces a magnetic field profile B.sub.01 (x) such that [B.sub.01 (x)].sup.2 =b.sub.1 -a.sub.1 x, where b.sub.1 and a.sub.1 are constants, for values of x in the range 0.6R<x<1.3R; this desired profile is provided within a cylindrical sample space indicated by the broken lines 4. Any nuclei with I=1 which are placed within this space will have precession rates and resonance frequencies .omega..sub.x which will vary as a linear function of the coordinate x, provided, where .eta.<0.1, that the ratio (GB cos .theta./ (.eta.K)).sup.2 is much less than one.

Detailed Description Text (4):
The arrangement of FIG. 1 will clearly require much less electrical power to establish a given range of magnetic field strengths than the arrangement of FIG. 2, but the fact that its sample space 4 lies mainly in the center of a coil and does not extend very far from the coil may be inconvenient for some applications. The FIG. 2 arrangement has the advantage that its useful sample space 8 is well separated from the coils and more accessible. This will make it more convenient for studies on human or animal patients. When the FIG. 2 configuration is used, it will be important to ensure that no part of the sample or body or any material which might have nuclear quadrupolar resonances in the frequency range being used should be present in the space where x<R, between the coils and the sample space 8, as this would produce confusing results in the same frequency range as the desired signal from the sample volume of the article or body under test.

Detailed Description Text (7):
FIGS. 3 and 4 show a front elevation and an end elevation of apparatus for NQR imaging using coils in the configurations of FIG. 1 and FIG. 2 to produce appropriate magnetic field gradients in three orthogonal directions. For the sake of clarity the end elevation FIG. 4 is drawn to a larger scale than the front elevation FIG. 3.

Detailed Description Text (9):
Two shielded electromagnet coils 21 and 22 are placed around the cylinder 16, to provide a magnetic field profile along the longitudinal direction of the rail 14, substantially in accordance with the principle of FIG. 1. The asymmetry of these coils should be noted; the smaller coil 22 is placed over the central part of cylinder 16 and the r.f. coils 17-20, and the larger coil 21 is displaced to one side by an amount equal to the mean radius of the coils.

Detailed Description Text (10):
Two concentric electromagnet coils 23 and 24 are supported in a horizontal plane centered just below the bottom of coil 22. The inner coil 24 is hidden by the outer coil 23. These coils will be used to provide a magnetic field profile in the vertical direction through the center of the volume within the cylinder 16. Two similar concentric coils 25 and 26 are mounted on a support structure 27, in a vertical plane immediately behind the coil 22. The inner coil 25 is hidden by the outer coil 26 in FIG. 4 and by the other components in FIG. 3. Both these coil pairs are arranged and used substantially in accordance with the principles of FIG. 2 but coil 23 is made a little smaller and coil 26 a little larger so that the rear of coil 23 can fit inside the lower part of coil 26. The coils 25 and 26 provide a magnetic field profile in a transverse horizontal direction. Positions within the sample space will be represented by orthogonal coordinates x, y and z in the directions indicated by axes Ox, Oy and Oz.

Detailed Description Text (11):
FIG. 5A-5C shows how the magnet currents may be varied in part of a typical cycle

of tests. The traces show the current i.sub.x passed through the coils 25 and 26, the current i.sub.y passed through coils 21 and 22, and the current i.sub.z passed through the coils 23 and 24. The part of the cycle shown comprises six scanning periods in which the currents are held constant, separated by transition periods in which one current is decreased while another is increased. Each current varies from zero to a maximum value I. The annotations below the scanning periods indicate the directions of the field gradients produced, the notation xy indicating a gradient along the direction of the line x=y, z=0. The time scale of the whole cycle in medical applications will be determined by the maximum allowable rate of change of magnetic field to avoid any risk of adverse effects. The whole cycle may typically take from one to ten minutes and will include several hundred scan periods.

Detailed Description Text (12):
During each scan period a pair of the r.f., coils will be excited with pulses at a repetition rate determined by the relaxation times of the quadrupole frequency to be detected and of relative phases determined by the nature of the pulse cycle. For example, one half of the excitation pulses in each scan period (preferably alternate pulses) may be phase-inverted. The resulting free induction decay and/or echo signals will be sampled and measured in sampling periods occurring at a set time after each excitation pulse and before the next excitation pulse. Preferably fast digital sampling is used to take many measurements in each sampling period. Measurements made at corresponding times are accumulated and averaged but the responses from the phase-inverted excitations are subtracted from the responses to the non-inverted excitations. Quadrature phase-sensitive detection may be used. As explained in the co-pending U.K. Patent Application No. 91 06789.2, this substantially distinguishes the free induction decay responses from the aftermath of the excitation pulses. The results from each scan period are then Fourier transformed to get a projection of the desired image along a line parallel to the magnetic field gradient. Conventional data-processing is then used to derive the desired image or images from the many projections produced from a cycle of scan periods. The temperature of the object needs to be known, so that the r.f. excitation frequency can be adjusted appropriately prior to imaging.

Detailed Description Text (13):
The excitation pulses may have a duration of about 25 to 150 .mu.s and the interval between consecutive excitation pulses .tau. may be in the range between 0.1T.sub.1 and 5T.sub.1 where T.sub.1 is the spin-lattice relaxation time constant for the quadrupole-frequency concerned. In a typical case this interval may be from 1 ms to 100 ms. In another application, the interval between pulses .tau. is set to be much less than T.sub.2 or T.sub.2e, the spin-spin relaxation times for the quadrupole frequency concerned; strong off-resonant phase-alternated pulses are used and the echo signals between pulses are accummulated as described above. With a suitable design for the r.f. coils the peak r.f. power required to irradiate a sample volume of 1/2 liter may be less than 1 kW. The free induction decay signals may be sampled at a rate of 1 MHz and a number of samples may be taken from each decay signal. For measurements on .sup.14 N nuclei in collagen at room temperature the resonance frequencies are about 2.196 MHz and 2.945 MHz. The .sup.14 N nuclei have resonance frequencies at about 2.160 MHz and 2.850 MHz. The corresponding quadruple coupling constants and asymmetry parameters are 3.43 MHz (0.44) and 3.34 MHz (0.41).

Detailed Description Text (15):
For imaging samples which may have significantly inhomogeneous temperature distributions, it is necessary to do tests with complementary magnetic field profiles. With some samples this may be done by inverting and rotating the article, or by rotating the coils 23,24,25 and 26 and their support structure through 180.degree. about a horizontal axis through the center of the sample space, but where this is inconvenient it may be desirable to provide extra magnet coils to produce complementary magnetic field profiles. The coils shown in FIGS. 3 and 4 will of course always provide higher field strength towards the left or bottom as shown in the drawings. The extra coils needed would be provided above, in front and

to the right of the sample space, symmetrical with the coils already shown in FIGS. 3 and 4. With appropriate precautions this form of the invention may be suitable for imaging parts of human limbs or even complete human or animal bodies.

Detailed Description Text (16):
FIG. 7 is a block circuit diagram showing electrical equipment for NQR imaging. A radiofrequency source 30 producing a single radiofrequency has normal and inverted-phase outputs connected through gates 31a and 31b to an r.f. power amplifier 32. Radiofrequency gate circuits 34 connect the power amplifier output to the r.f. coils 17,19 or 18,20 and also connect the r.f. coils through an r.f. preamplifier 35 and amplifier 36 to phase sensitive detectors 37a and 37b. The output of gates 31a and 31b is connected as a reference signal to the detector 37a and through a 90.degree. phase shift circuit to the detector 37b. Outputs from the detectors 37a and 37b are sampled and digitised by analogue to digital convertors 39a and 39b and then passed to a digital signal processor 40. Image information derived by the processor 40 is applied to a graphical recorder or video display 41. Timing circuits 42 control the gates 31a. 31b and 34 and also supply timing signals to the convertors 39a and 39b and the processor 40. The timing circuits 42 also control a filtered and stabilised power supply 43 which supplies and controls the currents in the magnet coils 21-22, 23-24 and 25-26.

Detailed Description Text (17):
For imaging nuclei in the particular circumstances described above where a linear magnetic field profile is required, this profile can be provided by coils in the anti-Helmholtz or Maxwell configuration--two coils of radius R, spaced R apart and connected to produce opposing fields. A system providing linear gradient fields in three orthogonal directions will have three pairs of identical coils symmetrically arranged about the sample space. In such a system complementary magnetic field profiles can be provided by simply reversing the direction of the currents. Such systems can provide a relatively inexpensive and simple method of imaging.

Detailed Description Text (19):
Suitable timing diagrams for putting this invention into effect are shown in FIGS. 8A-8D. The diagrams show excitations and excitation responses at two resonance frequencies. Referring to a first embodiment shown in FIG. 8A-8B, two radiofrequency pulses of width t.sub.w and of differing frequencies f.sub.1 and f.sub.2 are repeated at a pulse repetition time .tau. (.tau.>>t.sub.w) which is much longer than the spin-lattice relaxation time T.sub.1 --say .tau.=5T.sub.1 --to ensure full signal recovery between pulses; phase shifts of alternate pulses or suitable combinations of pulses of width t.sub.w and 2t.sub.w may be used to eliminate probe ringing. After phase-sensitive detection and manipulation of the appropriate signals during each repetition, the residual oscillations can be made to cancel and only the true NQR free induction decay (f.i.d.) response signals from the two resonances are observed The response signals are summed over the number of repetitions of the test. Sums from the two individual resonance frequencies may be maintained, or else a sum of all the response signals may be maintained. The pulses at the different frequencies are slightly staggered to avoid any problems with mixing due to non-linearities in the r.f. probe. However, the pulses could be simultaneous, or a frequency modulated or frequency swept (adiabatic) pulse could be utilised.

Detailed Description Text (24):
It will also be appreciated that, if the invention is applied just to detection of the presence of NQR substances rather than to imaging such substances, the digital signal processor 40 needs to be capable of processing the NQR response signals to produce an alarm signal in the appropriate circumstances. The magnet coils 21-22, 23-24 and 25-26 and the magnet power supply and control 43 would be unnecessary but a visual or audible alarm activated by the alarm signal would need to be provided.

Other Reference Publication (1):

E. Rommel et al., "Communications-Rotating Frame NQR Imaging," Journal of Magnetic Resonance 91, 1991, pp. 630-636.

Other Reference Publication (2):
S. Matsui et al., "Communicatons-An NQR Imaging Experiment on a Disordered Solid," Journal of Magnetic Resonance 88, 1990, pp. 186-191.

Other Reference Publication (6):
P.C. Lauterbur, "Image Formation By Induced Local Interactions: Examples Employing Nuclear Magnetic Resonance," Nature, vol. 242, Mar. 16, 1973, pp. 190-191.

Other Reference Publication (7):
Buess, et al., "NQR Detection Using a Meanderline Surface Coil", Journal of Magnetic Resonance 92, 1991, pp. 348-362.

CLAIMS:

1. A method of imaging within a sample space an object containing quadrupolar nuclei, comprising:

irradiating the object to excite nuclear quadruple resonance,

applying to the object a magnetic field gradient having a profile B such that B.sup.n varies linearly with distance, n being greater than one,

detecting resonance response signals from the nuclei, and

deriving an image from the response signals.

3. A method according to claim 1, wherein the magnetic field profile is produced by the combined effects of a central coil centered around the sample space and at least one offset coil coaxial with the central coil and offset to one side of the sample space, the total ampere-turns product of each offset coil being substantially greater than the ampere-turns product of the central coil, the fields of the offset coils and central coils acting in the same direction.

4. A method according to claim 1 wherein the magnetic field profile is produced by the combined effect of two coils of different diameters, both offset to one side of the sample space, the ampere-turns product of the larger coil being substantially greater than the ampere-turns product of the smaller coil, the field of the smaller coil opposing the field of the larger coil.

5. A method according to claim 1 further including:

detecting a variation of temperature within the sample space and comparing the results of a first set of tests with the magnetic field profile increasing in one direction and a second set of tests with the magnetic field profile increasing in an opposite direction.

6. A method according to claim 1 wherein tests are done in a sequence of magnetic field gradients in different directions and the image is derived by a projection-reconstruction method.

7. A method according to claim 6 wherein the magnetic field gradients are applied sequentially in at least three orthogonal directions.

8. A method according to claim 6 wherein the magnetic field gradients are applied sequentially in two orthogonal directions and the article is rotated incrementally about one of these directions during the sequence of tests.

9. A method for producing an image representing one of the distribution of a specific substance containing quadrupolar atomic nuclei of spin quantum number I.ltoreq.1 and local temperatures within a sample volume in an article, comprising:

irradiating the sample volume of the article with pulses of radio frequency electromagnetic energy at least close to a quadruple resonance frequency of the atomic nuclei in the presence of at least one magnetic field gradient having a profile which produces a variation of the resonance frequency which is substantially a linear function of distance in a direction of the magnetic field gradient within a sample volume of the article,

measuring response signals from the nuclei, and

deriving the image by data-processing the results of many such measurements, wherein the magnetic field profile is a function B.sub.o (x) of distance x such that its square (B.sub.o (x)).sup.2 is a linear function of x, within a limited sample volume of the article.

10. Apparatus for imaging within a sample space an object containing quadrupolar nuclei, comprising:

means for irradiating the object to excite nuclear quadruple resonance,

application means for applying to the object a magnetic field gradient having a profile B such that B.sup.n varies linearly with distance, n being greater than one,

means for detecting resonance response signals from the nuclei, and

means for deriving an image from the response signals.

17. Apparatus according to claim 10 wherein the application means includes at least two sets of electromagnetic coils arranged to provide magnetic field gradients in at least two orthogonal directions.

21. Apparatus for producing an image representing a distribution of a specific substance containing one of quadrupolar atomic nuclei of spin quantum number I.gtoreq.1 and local temperatures within a sample volume in an article, comprising:

means for irradiating a sample space with pulses of radio frequency electromagnetic energy at least close to a quadruple resonance frequency of the said atomic nuclei,

electromagnetic coils arranged for producing at least one magnetic field gradient across the sample space of a profile appropriate to produce a variation of the resonance frequency which will be a linear function of distance across the sample space in the direction of the magnetic field gradient,

means for measuring response signals from the atomic nuclei, and

data-processing means for deriving the image from the results of many such measurements, the electromagnetic coils being arranged to produce a magnetic field which is a function B.sub.o (x) of distance x such that its square (B.sub.o (x)).sup.2 is a linear function of x, within a limited sample volume of the article.

22. Apparatus according to claim 10 further comprising:

means for applying to the object a magnetic field gradient having a profile which varies linearly with distance.

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L11: Entry 12 of 17 File: USPT Sep 29, 1998

DOCUMENT-IDENTIFIER: US 5814989 A
TITLE: Methods and apparatus for NQR testing

Abstract Text (1):
A method and apparatus for imaging within a sample space an object containing quadrupolar nuclei comprises irradiating the object to excite nuclear quadrupole resonance, applying to the object a magnetic field gradient having a profile Bo(x) such that the square of the profile Bo(x))2 varies linearly with distance (x), detecting resonance response signals from the nuclei, and deriving an image from the response signals. A method of and apparatus for nuclear quadrupole resonance testing an object, and a method of and apparatus for detecting the presence of a particular substance containing a given species of quadrupolar nucleus, are also disclosed.

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Brief Summary Text (3):
The present invention relates to a method of and apparatus for imaging within a sample space an object containing quadrupolar nuclei. The object may, for instance, be a human or animal body or a part thereof; the image may be a simple spin-density image or may be a temperature, pressure or electric field distribution image. For convenience the imaging referred to above will be called NQR imaging. The present invention also relates to a method of and apparatus for NQR testing an object, and to a method of and apparatus for detecting the presence of a particular substance containing a given species of quadrupolar nucleus.

Brief Summary Text (5):
Methods for producing images from the resonances of spin-nuclei which have a magnetic moment but no electric quadrupole moment have been extensively developed and described in various books (e.g. P. Mansfield and P. G. Morris, "NMR Imaging in Biomedicine", 1982, Academic Press). Such methods may use linear magnetic field gradients superimposed on a strong, uniform magnetic field. The resonance frequencies of the spin-1/2 nuclei are linearly dependent on the total magnetic field; this is made to vary linearly with distance across the sample, and the distribution of the substance concerned is derived from the frequencies in the signals produced. Such techniques are commonly called NMR imaging.

Brief Summary Text (6):
Methods for imaging using the resonances of quadrupolar nuclei (which have Ill) would be expected to have several advantages. Firstly, the quadrupolar resonances can be detected without using the strong, uniform magnetic field which is needed to make the magnetic resonances of spin-1/2 nuclei conveniently detectable. Hence the relatively large, expensive and sample-size-limiting magnet structures which are necessary for NMR imaging will not be needed. Avoiding the need for this strong magnetic field also avoids the substantial complications and possible distortions caused by non-uniformity in the field and magnetic interference produced in

practical NMR equipment. Secondly, the quadrupolar resonances are more definitely or characteristically associated with specific chemical environments, and it is therefore easier to distinguish results which are due to a particular substance from effects which are due to other substances present in the sample. Methods in which quadrupolar resonances might be observed directly rather than through their interactions with magnetic resonances would be highly suitable for medical use because they do not require patients to be exposed to rapidly changing strong magnetic fields.

Brief Summary Text (7):
Possible disadvantages or limitations on NQR imaging are that the nuclei may be less abundant, may have nuclear quadrupole resonance frequencies lower than the magnetic resonance frequencies of the protons commonly used in NMR imaging, and may have smaller gyromagnetic ratios. This can create a sensitivity problem which has two aspects. Firstly, it may be difficult to achieve a degree of excitation of the quadrupolar nuclei comparable with the excitation of the spin-1/2 nuclei which is commonly used in NMR equipment. The radiofrequency power used in medical applications must be limited to avoid undue heating and damage to living tissue. Secondly, the response signals will be weak and of low signal-to-noise ratio, needing sophisticated data processing for their detection.

Brief Summary Text (8):
To our knowledge methods for imaging using quadrupolar resonances have as yet had very little development. Rommel et al (J. Magnetic Resonance 91, 630-636, 1991) reported theoretical reasoning with a conclusion that there would be great practical difficulties in any attempt to use such methods to derive any image from the interaction of a magnetic field gradient with quadrupolar nuclei, considering in particular half-integral spin nuclei of I.gtoreq.3/2. As an alternative, they reported a method in which the strength of a radiofrequency excitation was varied across a sample in zero magnetic field.

Brief Summary Text (9):
Matsui et al. (J. Magnetic Resonance 88, 186-191, 1990) reported measurements on .sup.35 Cl nuclei in sodium chlorate in a linear magnetic field, in which an image was derived from the effects of the field on the spectral shape and width of the resonance. It appears that this may be a special case; the .sup.35 Cl nuclei have I=3/2 and their asymmetry parameter in sodium chlorate is zero. Matsui et al. state that "it is practically impossible" for the magnetic field to shift the resonance frequency. This may be incorrect, at least in relation to nuclei other than .sup.35 Cl in substances other than sodium chlorate.

Brief Summary Text (11):
According to one aspect of the present invention, in general terms there are provided methods and apparatus for producing an image representing the distribution of a specific substance or local temperatures within an article or in part of a human or an animal body, wherein the article or apart of the body is irradiated with a pulse or pulses of radiofrequency energy at or close to a quadrupole resonance frequency of atomic nuclei of I.gtoreq.1 in the specific substance and is subjected to at least one magnetic field gradient having a profile which produces a variation (including possibly a splitting) of the resonance frequency which is a linear function of distance in the direction of the magnetic field gradient, response signals from the nuclei are measured and an image is derived by data processing the result of many such tests. According to the invention, preferably either the magnetic field profile is a function B.sub.0 (x) of distance x such that its square [B.sub.0 (x)].sup.2 is a linear function of x, within a limited sample volume of the article or body, or else the invention relates to a method of imaging using quadrupolar nuclei having integral spin quantum number (I=1, 2, 3, . . .), preferably having unity spin quantum number. .sup.14 N is a nucleus for which I=1.

Brief Summary Text (12):

According to an aspect of this invention, there is provided apparatus for imaging within a sample space an object containing quadrupolar nuclei, comprising means for irradiating the object to excite nuclear quadrupole resonance, means for applying to the object a magnetic field gradient having a profile B such that B.sup.n varies linearly with distance, n being greater than one, means for detecting resonance response signals from the nuclei, and means for deriving an image from the response signals.

Brief Summary Text (13):
The apparatus may further comprise means for applying to the object a magnetic field gradient having a profile which varies linearly with distance.

Brief Summary Text (14):
This invention arises from our discovery that, surprisingly, for a wide range of substances containing quadrupolar nuclei, a gradient profile having n greater than one (rather than a linear gradient) should be used in NQR imaging since it (rather than a linear gradient) produces a variation in resonance frequency which is a linear function of distance. As will be apparent from the following, for many (possibly the majority on applications we have discovered that n should be 2 (i.e. a square law gradient), by which is meant that n should be exactly, or close to, two.

Brief Summary Text (15):
Magnetic field gradients in different directions may be applied in sequence to derive sufficient results for the derivation of a two-dimensional or three-dimensional image, each gradient having a profile which makes the resonant frequency vary as a linear function of distance in the direction of the gradient. Where gradients in only two directions are used, the sample or article may be rotated about one of these directions to derive information sufficient for three-dimensional imaging.

Brief Summary Text (17):
The quadrupole resonance frequencies are also shifted by temperature variations, and by comparing tests with different magnetic field profiles the technique may be extended to produce images representing the variations of temperature in a sample or body part. This can provide a non-invasive method for measuring or monitoring localized temperatures within a sample or body part, and it may be useful in monitoring and/or controlling treatments which involve localized heating. Imaging of pressure or electric yield variations may be effected following the same principle.

Brief Summary Text (18):
In the sub-molecular environment of compounds or crystals, the nature and disposition of the adjacent electrons and atomic nuclei produce electric field gradients which modify the energy levels and the resonance frequencies of the quadrupolar nuclei. The symmetry or asymmetry of these local electric field gradients is an important factor in any study of nuclear quadrupole resonance, and it is measured by an asymmetry parameter .eta. which can have values from zero to one. For instance, for the ring nitrogen in the explosive RDX, .eta..apprxeq.0.62, whilst for the peptide nitrogen in amino acids and polypeptides .eta..apprxeq.0.4; the nitrogen in cocaine and heroin is thought to have .eta..ltoreq.0.1. The spin quantum number .sup.- I is another controlling factor. .sup.14 N and .sup.2 H nuclei have I=1; nuclei such as .sup.11 B and .sup.75 As have I=3/2, and .sup.17 O and .sup.27 Al I=5/2, etc.

Brief Summary Text (20):
When first and second-order perturbation theory are applied to a study of these resonance frequencies in an externally applied magnetic field, it appears that there are substantially two cases which can be represented by different mathematical approximations.

Brief Summary Text (21):
For such nuclei in substances having .eta.>0.1, over a considerable range of magnetic field strengths the resonance frequencies of individual nuclei may be expressed by equations, derived from a paper by S. Pissanetzky (Zeeman effect of .sup.14 N nuclear quadrupole resonance with polycrystalline samples, J. Chem. Phys., Vol. 59, No. 8, p. 4197, 1973), of the form

Brief Summary Text (22):
where G=.gamma./2.pi.. .gamma.=the gyromagnetic ratio, and K=.vertline.e.sup.2 qQ/4h.vertline., e.sup.2 qQ/h being the quadrupole coupling constant. F.sub.x, F.sub.y and F.sub.z are functions involving .eta. and the two polar angles (.theta., .phi.) specifying the relative orientation of the local electric field gradient with respect to the direction of the applied magnetic field B. Since in general there will be many molecules randomly oriented with respect to the direction of the applied magnetic field, there will be many nuclei with a range of values of F.sub.x, F.sub.y and F.sub.z and consequently a range of resonant frequencies from each location with any non-zero value of B: the resonance is broadened. However, the maximum value of the dominant term in the expressions for F.sub.x, F.sub.y and F.sub.z is proportional to 1/.eta., and hence this broadening is comparatively limited for substances which have a relatively high asymmetry parameter .eta..

Brief Summary Text (23):
It is possible with much computation to calculate how the resonances of a population of randomly-oriented nuclei will combine to determine the line shape and frequency shift of their observable resonance effect.

Brief Summary Text (24):
The results of our researches are that, in general, the observable resonances will show a frequency shift proportional to B.sup.2 with a gradual broadening of the line shape, until a critical field strength, B.sub.2 is reached; above this field strength the line shape becomes distorted and the frequency shift gradually departs from a strict B.sup.2 dependence. The angle .alpha. between the directions of the magnetic field B and the radiofrequency excitation field B.sub.1 has a significant effect on the onset and nature of these changes, and it affects different lines differently.

Brief Summary Text (25):
He have conducted experiments using pure substances in a uniform magnetic field of adjustable strength to study how the field strength alters the line shape and shift. From such experiments using samples of various explosives containing .sup.4 N nuclei such as RDX (for the ring .sup.14 N of which .eta.=0.62), we have found that the resonant frequency .omega..sub.x does shift in proportion to B over a substantial range of magnetic field strengths. We have also found that above a certain field strength, the resonances we have studied develop a doublet structure when B is perpendicular to B.sub.1. Fine structure is also indicated in the results published by Matsui at al. though they did not comment on it. In the case of RDX, both components of the doublet shift in proportion to B.sup.2, with different rates; we would expect the same to be true for other substances.

Brief Summary Text (26):
Hence for NQR imaging of nuclei having I=1 in substances having .eta.>0.1, it is preferable to use a magnetic field profile B(x) such that

Brief Summary Text (33):
Hence, for a majority of the substances of practical interest with nuclei having integral spin quantum number, a magnetic field profile of the form given in Equation 5 is appropriate.

Brief Summary Text (34):
However, there may be some substances for which (GB cos .theta./(.eta.K)).sup.2 is near unity and for which therefore the above analysis does not hold. Sometimes, dependent on the substance, a profile substantially of the form given in Equation 5 would still be appropriate, with any slight deviations from a precise B.sup.2 dependence being accommodated by appropriate minor adjustments to the field gradient profile to give a linear frequency shift. In other circumstances the deviations from a B.sup.2 dependence may be so significant that a completely different gradient profile may need to be employed. Such a profile would normally be somewhere between square law and linear (that is, 1<n<2, where n is the power of the profile referred to previously), although there may be some cases where .eta. is actually greater than two.

Brief Summary Text (35):
The case of nuclei having half integral spin quantum number is now considered. I=3/2 nuclei are taken as a representative example, but the principles behind the following analysis, and the conclusions drawn from the analysis, apply to all half integral spin systems. Nuclei with I=3/2 in a single crystal structure in a weak magnetic field B have four quadrupole resonance frequencies given by equations of the form

Brief Summary Text (36):
where E is a function of .gamma. and .eta. and the four resonances have different functions F.sub.n. This leads for single crystals to frequency shifts linearly dependent on the magnetic field strength B.

Brief Summary Text (37):
Hence, a linear magnetic field profile will be appropriate for imaging nuclei with I=1, 2, 3 . . . etc. when (GB cos .theta./(.eta.K)).sup.2 >>1 or nuclei with I=3/2, etc. in a single crystal structure. This can be provided by coils in the anti-Helmholtz or Maxwell configuration--two coils of radius R, spaced R apart and connected to produce opposing fields. A system providing linear gradient fields in three orthogonal directions will have three pairs of identical coils symmetrically arranged about the sample space. In such a system complementary magnetic field profiles can be provided by simply reversing the direction of the currents. Such systems may be suitable, for instance, for the imaging of parts of human arms or legs and possibly heads; they should be simpler and less expensive than present NMR imaging instruments.

Brief Summary Text (38):
For substances with I=3/2, 5/2, etc. other than single crystal structures, the dependence of resonance frequency on magnetic field becomes complex and not readily amenable to theoretical analysis. In these circumstances, we propose that the relationship between resonance frequency and magnetic field is predetermined for a specific substance of interest and stored as a "look-up" table. Then a magnetic field profile of the form given in Equation 5 (or otherwise a linear field gradient) may be employed to produce spatial encoding. The image can be derived by appropriate use of the look-up table. Alternatively, a field profile, such as would produce a variation of resonance frequency which is substantially a linear function of distance in the direction of the magnetic field gradient, could be utilised. This profile would usually have a form somewhere between linear and square law (that is, 1<n<2).

Brief Summary Text (39):
By employing the magnetic field profiles described above known methods of NMR imaging can be adapted to NQR imaging, the major simplification being the elimination of the strong background magnetic field which is necessary for NMR experiments.

Brief Summary Text (40):

In NMR imaging, it is usual to use radiofrequency pulses of sufficient power to cause a 90.degree. rotation of the magnetisation of the nuclei. The pulse duration t.sub.w is given by the equation ##EQU1## where B.sub.1 is the peak strength of the radio frequency excitation field. There will be other constraints on the pulse duration and so in effect this equation often sets the power required. In NQR experiments the corresponding condition for polycrystalline samples containing spin-1 nuclei is ##EQU2##

Brief Summary Text (41):
The gyromagnetic ratio .gamma. will usually be much smaller for quadrupole nuclei than for protons, so that the r.f. field strength and power required to satisfy equation (11) will be much greater than that required to achieve the corresponding conditions in NMR imaging of protons. Hence it may be practically preferable or necessary to use pulses of considerably lower power and rotation angle, and to make up for this by accumulating results from more pulses, and probably applying pulses more frequently, so that the interval between pulses (.tau.) is less than the spin-lattice relaxation time (T.sub.1). This may be particularly necessary to avoid tissue damage in medical applications. This will also make the accumulated signal strength less sensitive to variations in the rotation angle over the sample space. Shaped or phase/amplitude modulated pulses can also assist in reducing the r.f. power.

Brief Summary Text (42):
The projection-reconstruction methods of imaging developed from the work of Lauterbur (Nature 242, 190-191, Mar. 16, 1973) may be preferred for medical applications as they require only small step-wise changes in the magnetic field gradients.

Brief Summary Text (43):
Variations of temperature may cause frequency shifts comparable with the frequency shifts caused by the magnetic field. This will cause distortion in images of samples which have an inhomogeneous temperature distribution, but this can be corrected. This effect may also be used to advantage as a non-invasive means for imaging or monitoring the temperature distribution within the sample. Over a small temperature range, the variation in frequency is often linear with respect to temperature.

Brief Summary Text (44):
Fourier transformation of a set of results taken in zero magnetic field with a sufficiently short r.f. pulse will therefore give a spectrum which, when compared with one or more spectra of a homogenous uniform temperature sample of the relevant substance, will indicate the range of temperatures present.

Brief Summary Text (45):
Increasing temperature generally shifts the resonances to a lower frequency, so that in any image produced by excitation of the frequency .omega..sub.x without temperature correction, indications of the nuclear density in any hot spot will appear displaced towards the region of lower magnetic field. Repeating the experiment with the field profile reversed (or complementary) will cause the hot-spot signal to appear displaced in the opposite direction, and comparison with the previous image will indicate the position of the hot spot and its temperature.

Brief Summary Text (46):
Variations of pressure or electric field will also cause frequency shifts which may be utilized for imaging purposes.

Brief Summary Text (47):
Where the magnetic field splits any resonance into a multiplet, or where there are two or more resonant frequencies close together, it is advantageous to use excitation signals having a frequency distribution broad enough to excite all

resonances or all parts of the multiplet. The response signals will then show a pattern of slow beats at the difference frequencies. In certain cases, e.g. when the line is a simple doublet, it may be desirable to use the frequency of these slow beats as the characteristic to be measured, rather than the frequency of either resonance, because it will usually be more sensitive to variations in field strength and it may be more readily distinguishable.

Brief Summary Text (58):
Preferably, the resonance frequencies are components of a multiplet. A multiplet usually connotes two or more resonance frequencies which are relatively close together (usually within a few percent of each other) and are yet well-resolved. Multiplets may arise, for instance, due to crystallographic non-equivalence of otherwise structurally identical NQR nuclei (as is the case with, for example, RDX, TNT and HMX); they may also arise (e.g. Heroin and Cocaine) due to the nearly axially symmetric electric field gradient in which the NQR nuclei are located.

Brief Summary Text (64):
Preferably, the alarm signal is provided in further dependence on whether the relative intensities of the response signals at each of the plurality of resonance frequencies match those which would be expected for the particular substance. This measure can further reduce the number of false positives. It is envisaged that this measure may suitably be put into practice by predetermining in separate tests the relevant characteristics of the particular substance and storing these for use in the field.

Brief Summary Text (66):
Since resonance frequency varies with temperature, pressure or magnetic field, it may be necessary to take such variations into account by irradiating over a range sufficient to cover all possible variations of resonance frequency which might in practice be encountered.

Brief Summary Text (68):
In the case of RDX (cyclo-trimethylenetrinitramine) the multiplicity produced by crystallographic non-equivalence of otherwise structurally identical nitrogen nuclei can be exploited. In the vapor phase, the molecule is said to have C.sub.3.upsilon. symmetry, but this is lost in the solid state, and all three .sup.14 N quadrupole resonance lines from the ring nitrogen nuclei are well-resolved triplets. The splittings are small (less than 150 kHz for .upsilon..sub.x near 5,100 kHz), and, although the individual frequencies vary with temperature, the splittings themselves are almost independent of temperature between -30.degree. and +30.degree. C., varying from 143,52 kHz at the former to 145,49 kHz at the latter.

Brief Summary Text (70):
After each pulse or pulse sequence at a given frequency, the NQR instrument will analyse the absorption peak for its frequency, height, width and area, taking into account possible errors assessed from the noise measured off-resonance. In this example, only if statistically equivalent responses are detected after each excitation frequency has been excited would the instrument provide an alarm signal.

Brief Summary Text (71):
The above technique can be highly discriminatory against noise peaks and interference; only RDX will give equal, or nearly equal, response signals at the three selected frequencies at a given temperature.

Brief Summary Text (72):
Heroin and Cocaine are now considered. We have discovered that Heroin shows a close doublet (.upsilon..sub.x, .upsilon..sub.y) near 3,900 kHz and Cocaine a doublet near 960 kHz. In these cases, the splitting arises from the nearly-axially

symmetric electric field gradient in which the .sup.14 N nucleus is located, and not from resolved crystallographic non-equivalence. The present invention still applies, and the signal-to-noise ratio may be increased by .sqroot.2 in these two cases, although the lines are not completely independent.

Drawing Description Text (3):
FIGS. 1 and 2 are diagrammatic representations of alternative electromagnet coil configurations which may be used to produce a magnetic field profile B(x) such that [B(x)].sup.2 varies as a linear function of distance x;

Detailed Description Text (2):
FIG. 1 shows in axial section two coils 1 and 2 which have the same mean radius R and are spaced a distance R apart on a common axes 3. Coil 1 will have twice the ampere-turns (ni) of coil 2, the current directions being the same so that their fields are in the same direction. If distance along the axis from the plane of coil 1 is denoted by x, this arrangement produces a magnetic field profile B.sub.01 (x) such that [B.sub.01 (x)].sup.2 =b.sub.1 -a.sub.1 x, where b.sub.1 and a.sub.1 are constants, for values of x in the range 0.6R<x<1.3R; this desired profile is provided within a cylindrical sample space indicated by the broken lines 4. Any nuclei with I=1 which are placed within this space will have precession rates and resonance frequencies .omega..sub.x which will vary as a linear function of the coordinate x, provided, where n<0.1, that the ratio (GB cos .theta./(.eta.K)).sup.2 is much less than one.

Detailed Description Text (4):
The arrangement of FIG. 1 will clearly require much less electrical power to establish a given range of magnetic field strengths than the arrangement of FIG. 2, but the fact that its sample space 4 lies mainly in the center of a coil and does not extend very far from the coil may be inconvenient for some applications. The FIG. 2 arrangement has the advantage that its useful sample space 8 is well separated from the coils and more accessible. This will make it more convenient for studies on human or animal patients. When the FIG. 2 configuration is used, it will be important to ensure that no part of the sample or body or any material which might have nuclear quadrupolar resonances in the frequency range being used should be present in the space where x<R, between the coils and the sample space 8, as this would produce confusing results in the same frequency range as the desired signal from the sample volume of the article or body under test.

Detailed Description Text (7):
FIGS. 3 and 4 show a front elevation and an end elevation of apparatus for NQR imaging using coils in the configurations of FIG. 1 and FIG. 2 to produce appropriate magnetic field gradients in three orthogonal directions. For the sake of clarity the end elevation FIG. 4 Is drawn to a larger scale than the front elevation FIG. 3.

Detailed Description Text (9):
Two shielded electromagnet coils 21 and 22 are placed around the cylinder 16, to provide a magnetic field profile along the longitudinal direction of the rail 14, substantially in accordance with the principle of FIG. 1. The asymmetry of these coils should be noted; the smaller coil 22 is placed over the central part of cylinder 16 and the r.f. coils 17-20, and the larger coil 21 is displaced to one side by an amount equal to the mean radius of the coils.

Detailed Description Text (10):
Two concentric electromagnet coils 23 and 24 are supported in a horizontal plane centred just below the bottom of coil 22. The inner coil 24 is hidden by the outer coil 23. These coils will be used to provide a magnetic field profile in the vertical direction through the centre of the volume within the cylinder 16. Two similar concentric coils 25 and 26 are mounted on a support structure 27 in a vertical plane immediately behind the coil 22. The inner coil 25 is hidden by the

outer coil 26 in FIG. 4 and by the other components in FIG. 3. Both these coil pairs are arranged and used substantially in accordance with the principles of FIG. 2 but coil 23 is made a little smaller and coil 26 a little larger so that the rear of coil 23 can fit inside the lower part of coil 26. The coils 25 and 26 provide a magnetic field profile in a transverse horizontal direction. Positions within the sample space will be represented by orthogonal coordinates x, y and z in the directions indicated by axes Ox, Oy and Oz.

Detailed Description Text (11):
FIGS. 5A-5C show how the magnet currents may be varied in part of a typical cycle of tests. The traces show the current i.sub.x passed through the coils 25 and 26, the current i.sub.y passed through coils 21 and 22, and the current i.sub.z passed through the coils 23 and 24. The part of the cycle shown comprises six scanning periods in which the currents are held constant, separated by transition periods in which one current is decreased while another is increased. Each current varies from zero to a maximum value I. The annotations below the scanning periods indicate the directions of the field gradients produced, the notation xy indicating a gradient along the direction of the line x=y, z=0. The time scale of the whole cycle in medical applications will be determined by the maximum allowable rate of change of magnetic field to avoid any risk of adverse effects. The whole cycle may typically take from one to ten minutes and will include several hundred scan periods.

Detailed Description Text (12):
During each scan period, a pair of the r.f. coils will be excited with pulses at a repetition rate determined by the relaxation times of the quadrupole frequency to be detected and of relative phases determined by the nature of the pulse cycle. For example, one half of the excitation pulses in each scan period (preferably alternate pulses) may be phase-inverted. The resulting free induction decay and/or echo signals will be sampled and measured in sampling periods occurring at a set time after each excitation pulse and before the next excitation pulse. Preferably fast digital sampling is used to take many measurements in each sampling period. Measurements made at corresponding times are accumulated and averaged but the responses from the phase-inverted excitations are subtracted from the responses to the non-inverted excitations. Quadrature phase-sensitive detection may be used. As explained in the co-pending U.K. Patent Application No. 91 06789.2, this substantially distinguishes the free induction decay responses from the aftermath of the excitation pulses. The results from each scan period are then Fourier transformed to get a projection of the desired image along a line parallel to the magnetic field gradient. Conventional data-processing is then used to derive the desired image or images from the many projections produced from a cycle of scan periods. The temperature of the object needs to be known, so that the r.f. excitation frequency can be adjusted appropriately prior to imaging.

Detailed Description Text (13):
The excitation pulses may have a duration of about 25 to 150 .mu.s and the interval between consecutive excitation pulses .tau. may be in the range between 0.1T.sub.1 and 5T.sub.1 where T.sub.1 is the spin-lattice relaxation time constant for the quadrupole-frequency concerned. In a typical case this interval may be from 1 ms to 100 ms. In another application, the interval between pulses .tau. is set to be much less than T.sub.2 or T.sub.2e, the spin-spin relaxation times for the quadrupole frequency concerned; strong off-resonant phase-alternated pulses are used and the echo signals between pulses are accummulated as described above. With a suitable design for the r.f. coils the peak r.f. power required to irradiate a sample volume of 1/2 liter may be less than 1 kW. The free induction decay signals may be sampled at a rate of 1 MHz and a number of samples may be taken from each decay signal. For measurements on .sup.14 N nuclei in collagen at room temperature the resonance frequencies are about 2.196 MHz and 2.945 MHz. The .sup.14 N nuclei have resonance frequencies at about 2.160 MHz and 2.850 MHz. The corresponding quadruple coupling constants and asymmetry parameters are 3.43 MHz (0.44) and 3.34 MHz (0.41).

Detailed Description Text (15):
For imaging samples which may have significantly inhomogeneous temperature distributions, it is necessary to do tests with complementary magnetic field profiles. With some samples this may be done by inverting and rotating the article, or by rotating the coils 23,24,25 and 26 and their support structure through 180.degree. about a horizontal axis through the center of the sample space, but where this is inconvenient it may be desirable to provide extra magnet coils to produce complementary magnetic field profiles. The coils shown in FIGS. 3 and 4 will of course always provide higher field strength towards the left or bottom as shown in the drawings. The extra coils needed would be provided above, in front and to the right of the sample space, symmetrical with the coils already shown in FIGS. 3 and 4. With appropriate precautions this form of the invention may be suitable for imaging parts of human limbs or even complete human or animal bodies.

Detailed Description Text (16):
FIG. 7 is a block circuit diagram showing electrical equipment for NQR imaging. A radiofrequency source 30 producing a single radiofrequency has normal and inverted-phase outputs connected through gates 31a and 31b to an r.f. power amplifier 32. Radiofrequency gate circuits 34 connect the power amplifier output to the r.f. coils 17,19 or 18,20 and also connect the r.f. coils through an r.f. preamplifier 35 and amplifier 36 to phase sensitive detectors 37a and 37b. The output of gates 31a and 31b is connected as a reference signal to the detector 37a and through a 90.degree. phase shift circuit to the detector 37b. Outputs from the detectors 37a and 37b are sampled and digitised by analogue to digital convertors 39a and 39b and then passed to a digital signal processor 40. Image information derived by the processor 40 is applied to a graphical recorder or video display 41. Timing circuits 42 control the gates 31a, 31b and 34 and also supply timing signals to the convertors 39a and 39b and the processor 40. The timing circuits 42 also control a filtered and stabilised power supply 43 which supplies and controls the currents in the magnet coils 21-22, 23-24 and 25-26.

Detailed Description Text (17):
For imaging nuclei in the particular circumstances described above where a linear magnetic field profile is required, this profile can be provided by coils in the anti-Helmholtz or Maxwell configuration--two coils of radius R, spaced R apart and connected to produce opposing fields. A system providing linear gradient fields in three orthogonal directions will have three pairs of identical coils symmetrically arranged about the sample space. In such a system, complementary magnetic field profiles can be provided by simply reversing the direction of the currents. Such systems can provide a relatively inexpensive and simple method of imaging.

Detailed Description Text (19):
Suitable timing diagrams for putting this invention into effect are shown in FIGS. 8A-8D. The diagrams show excitations and excitation responses at two resonance frequencies. Referring to a first embodiment shown in FIGS. 8A-8B, two radiofreauency pulses of width t.sub.w and of differing frequencies f.sub.1 and f.sub.2 are repeated at a pulse repetition time .tau. (.tau.>>t.sub.w) which is much longer than the spin-lattice relaxation time T.sub.1 --say .tau.=5T.sub.1 --to ensure full signal recovery between pulses; phase shifts of alternate pulses or suitable combinations of pulses of width t.sub.w and 2t.sub.w may be used to eliminate probe ringing. After phase-sensitive detection and manipulation of the appropriate signals during each repetition, the residual oscillations can be made to cancel and only the true NQR free induction decay (f.i.d.) response signals from the two resonances are observed. The response signals are summed over the number of repetitions of the test. Sums from the two individual resonance frequencies may be maintained, or else a sum of all the response signals may be maintained. The pulses at the different frequencies are slightly staggered to avoid any problems with mixing due to non-linearities in the r.f. probe. However, the pulses could be simultaneous, or a frequency modulated or frequency swept (adiabatic) pulse could be utilised.

Detailed Description Text (23):
It will also be appreciated that, if the invention is applied just to detection of the presence of NQR substances rather than to imaging such substances, the digital signal processor 40 needs to be capable of processing the NQR response signals to produce an alarm signal in the appropriate circumstances. The magnet coils 21-22, 23-24 and 25-26 and the magnet power supply and control 43 would be unnecessary but a visual or audible alarm activated by the alarm signal would need to be provided.

Other Reference Publication (3):
Journal of Magnetic Resonance vol. 88, No. 1 1 Jun. 1990, Orlando, MN, US, pp. 186-191, S. Matsui et al. Experiment on a Disordered Solid.

Other Reference Publication (4):
Journal of Magnetic Resonance, vol. 91, No. 3, 15 Feb. 1991, Orlando, MN, US, pp. 630-636 E. Rommel et al."Rotating-Frame NQR Imaging".

Other Reference Publication (5):
Journal of Magnetic Resonance, vol. 92, No. 2, 1 Apr. 1991, Orlando, MN. US, pp. 348-362. M.L. Buess et al "NQR Detection Using a Meanderline Surface Coil".

Other Reference Publication (7):
WO,A, 9 217 793 (British Technology Group Limited) 15 Oct. 1992 see Abstract , see p. 2, line 6 - line 28, see p. 3, line 5 - line 10 & see P. 6, line 12 - line 33.

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